EXHIBIT 13

US006146361A

United States Patent [19]

DiBiasi et al.

[11] Patent Number: 6,146,361

[45] Date of Patent: *Nov. 14, 2000

[54] **MEDICATION DELIVERY PEN HAVING A 31 GAUGE NEEDLE**

[75] Inventors: **Michael D. DiBiasi**, West Milford; **Elizabeth A. Harbin**, Wayne; **Robert E. West**, Morristown, all of N.J.

[73] Assignee: **Becton Dickinson and Company**, Franklin Lakes, N.J.

[*] Notice: This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

[21] Appl. No.: **08/721,368**

[22] Filed: **Sep. 26, 1996**

[51] **Int. Cl.**[7] **A61M 5/00**

[52] **U.S. Cl.** **604/232**; 604/272

[58] **Field of Search** 604/232, 233, 604/234, 272, 207, 208, 211, 187

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,313,439	2/1982	Babb et al.	128/214
4,552,561	11/1985	Eckenhoff	604/896
4,692,142	9/1987	Dignam et al.	604/117
4,894,054	1/1990	Miskinyar	604/136
4,917,670	4/1990	Hurley et al.	604/51
4,944,677	7/1990	Alexandre	433/165
4,969,884	11/1990	Yum	604/892
4,973,318	11/1990	Holm	604/208
5,015,235	5/1991	Crossman	604/117
5,151,093	9/1992	Theeuwes et al.	604/892
5,279,586	1/1994	Balkwill	604/232 X
5,295,976	3/1994	Harris	604/211
5,374,256	12/1994	Kriesel	604/232
5,462,535	10/1995	Bonnichsen et al.	604/272
5,540,657	7/1996	Kurjan et al.	604/117
5,599,323	2/1997	Bonnichsen et al.	604/272
5,709,668	1/1998	Wacks	604/232
5,951,530	4/1999	Steengaard et al.	604/272
5,984,906	11/1999	Bonnichsen et al.	604/272

FOREIGN PATENT DOCUMENTS

0 702 970	3/1996	European Pat. Off. .
3-275214	12/1991	Japan .
4-502877	5/1992	Japan .
6-86745	12/1994	Japan .
WO90/07348	7/1990	WIPO .
WO 92/17131	10/1992	WIPO .
WO 93/00948	1/1993	WIPO .
WO 93/07877	4/1993	WIPO .
WO93/07922	4/1993	WIPO .
WO95/12425	5/1995	WIPO .

OTHER PUBLICATIONS

Applied Radiology, Jun. 1994, vol. 23, No. 6., advertisement for Ranfac corporation.

The Journal of Pharmacology and Experimental Therapeutics, Dorothea E. Blandford et al., "Role of Vasopressin in Response to Intrarenal Infusions of Alpha–2 Adrenoceptor Agonists", vol. 255, No. 1 (1990).

The Journal of Pharmacology and Experimental Therapeutics, D.D. Smyth et al., Opposite Rank Order of Potency for Alpha–2 Adrenoceptor Agonists on Water and Solute Excretion in the Rat: Two Sites and/or Receptors; vol. 261, No. 3 (1992).

BMJ, "Insulin Injection Technique", Jonathan Thow, et al., vol. 301, Jul. 7, 1990.

Diabetes Care, Anders Frid, et al., "Effects of Accidental Intramuscular Injection on Insulin Absorption in IDDM", 1988, vol. 11, pp. 41–45.

Diabetic Medicine, J.C. Thow, et al., "Insulin Injection Site Tissue Depths and Localization of a Simulated Insulin Bolus Using a Novel Air Contrast Ultrasonographic Technique in Insulin Treated Diabetic Subjects", 1992, pp. 915–920.

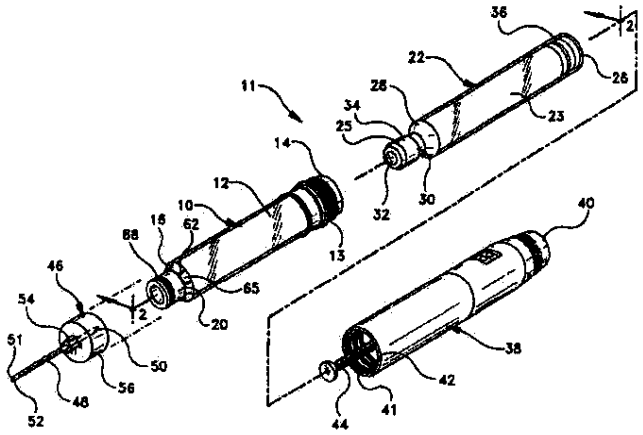
(List continued on next page.)

Primary Examiner—John D. Yasko
Attorney, Agent, or Firm—Alan W. Fiedler

[57] **ABSTRACT**

A needle assembly for a medication delivery pen having a 31 gauge needle cannula that reduces penetration force during an injection process resulting in less pain to the patient without causing any loss in performance or structural integrity.

9 Claims, 2 Drawing Sheets



OTHER PUBLICATIONS

Diabetes Care, Per Hildebrandt, et al., "The Absorption of Subcutaneously Injected Short–Acting Soluble Insulin: Influence of Injection Technique and Concentration", 1983, vol. 6, pp. 459–462.

Diabetic Medicine, A. Vaag, et al., "Intramuscular Versus Subcutaneous Injection of Unmodified Insulin: Consequences for Blood Glucose Control in Patients with Type 1 Diabetes Mellitus", 1990, pp. 335–342.

Diabetes Care, Allan Vaag, et al, "Variation in Absorption of NPH Insulin", 1990, vol. 13, pp. 74–76.

Scand J. Caring Science, Lars Engstrom, et al., "Short Communication", 1993, pp. 57–59.

Diabetes Care, Jiten P. Vora, et al., "Relationship Between Absorption of Radiolabeled Soluble Insulin, Subcutaneous Blood Flow, and Anthropometry", 1992, vol. 15, pp. 1484–1493.

Archives of Disease in Childhood, C.P. Smith, et al., "Subcutaneous or Intramuscular Insulin Injections", 1991, pp. 879–882.

Diabetic Medicine, P.H.E.M. de Meijer, et al., "The Variability of Absorption of Subcutaneously Injected Insulin: Effect of Injection Technique and Relation with Brittleness", 1990, pp. 499–505.

Diabetes Care, Michel Polak, et al, "Subcutaneous or Intramuscular Injections of Insulin in Children", 1996, vol. 19, pp. 1434–1436.

Diabetic Medicine, J.C. Thow, et al., "Different Absorption of Isophase (NPH) Insulin from Subcutaneous and Intramuscular Sites Suggests a Need to Reassess Recommended Insulin Injection Technique", 1990 pp. 600–602.

Diabetic Medicine, J.E. Henriksen, et al, "Absorption of NPH (Isophane) Insulin in Resting Diabetic Patients: Evidence for Subcutaneous Injection in the Thigh as the Preferred Site", 1991, pp. 453–457.

Diabetes Care, John P. Bantle, et al., "Effects of the Anatomical Region Used for Insulin Injections on Glycemia in Type I Diabetes Subjects", 1993, vol. 16, pp. 1592–1596.

Diabetologia, J.E. Henriksen, et al., "Impact of Injection Sites for Soluble Insulin on Glycaemic Control Type 1 (insulin–dependent) Diabetic Patients Treated with a Multiple Insulin Injection Regimen", 1993, pp. 752–758.

Opinion & Order, 96 Civ. 9506 (BSJ), Mar. 9, 1998 (USDC, SDNY). Hypodermic Disposable Needles: Mechanical Properties and Pain Perception as a Function of Needle Diameter: Lene Lytzen Jun. 1991

Photocopy of package for Terumo needle sold in 1989, having needle internal diameter 0.13 to 0.15 mm.

"Announcing The New Micro–Fine IV Pen Needle", pp. BD386–BD 389, published Jul. 1, 1991.

Australian Standard 2145–1985, "Hypodermic Equipment––Hypodermic Needle Tubing", published by The Standards Association of Australia, Jul. 12, 1985, pp. 24–37.

NovoFine 30G 8mm, "NovoFine reduces pain and the risk of intramuscular injections", pp. 18.1–18.4, May, 1993.

United States Court of Appeals for the Federal Circuit Civil Action 98–1312,–1313, Novo Nordisk A/S, Novo Nordisk of North America, Inc., and Novo Nordisk Pharmaceuticals, Inc., v. Eli Lilly and Co., and Becton Dickinson and Company, Decided Feb. 23, 1999.

Insuject–Insuject–X, The Insulin Pens From Nordisk–Wellcome, Freedom of Choice–Freedom of Lifestyle, pp. BD 17378–17383, –BD 17395, c. 1988–1989.

Novolin Pen, Dial–A–Dose Insulin Delivery System, Teaching Manual, Squibb Novo, pp. BD 15360–BD 15373, 1988.

Brochure, "The Outstanding Insulin Cartridge for the Insuject System", BD 017384–BD 017395, c. 1988–1989.

Novo Nordisk A/S, Novo Nordisk of North America, Inc. and Novo Nordisk Pharmaceuticals Inc. v. Becton Dickinson and Company, 96 Civ. 9506 (BSJ), Declarations of Arthur D. Dawson, Ph.D, Red Cassel, and Justin Boylan, and attached Exhibits 47–49.

International Standard, ISO 9626, "Stainless Steel Needle Tubing for Manufacture of Medical Devices ", pp. 2630–2639; Sep. 1, 1991.

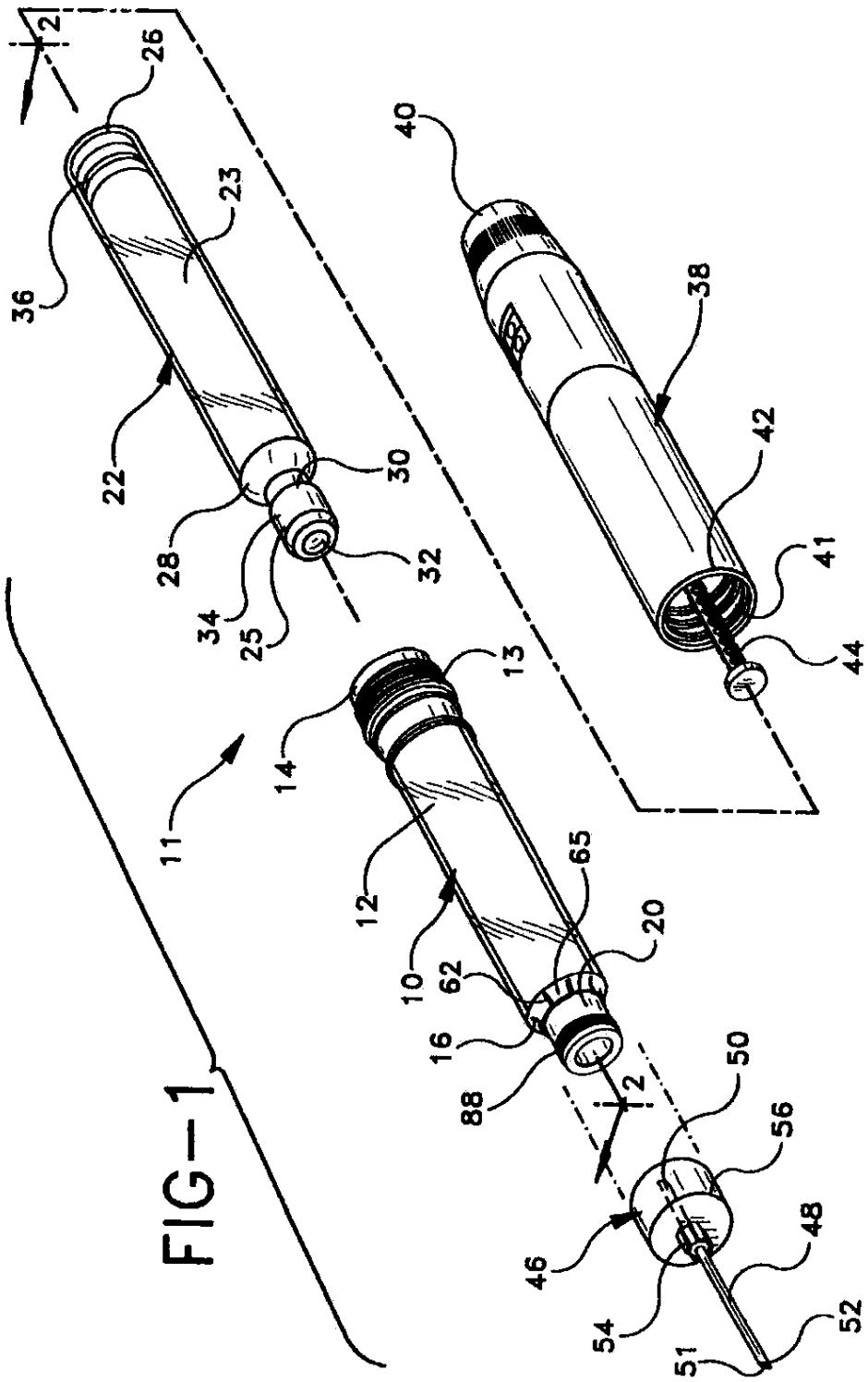
The Advanced Approach to Insulin Injection, The Individually Adapted and Flexible Insulin Therapy, BD 000551–BD 000554, Jun., 1987.

"State–of–the–art, Injection Technology from Switzerland", BD000555–000558, 1998.

Advertising Brochure for Terumo 29 Gauge Insulin Syringe, Diabetes Educator, Jan.–Feb. 1989, p. Nov 0034718.

Product Information, Terumo Insulin Syringe, published c. 1989, p. Nov. 0034714.

Novo Nordisk internal memorandum dated Oct. 23, 1989 re: testing of Terumo 29 gauge syringes having measured inner diameter of 0.13–0.15mm.


2
26
23
36
22
28
34
25
30
32
40
38
42
41
44
13
14
11
12
65
20
10
62
16
88
2
50
56
48
46
54
51
52

FIG—1

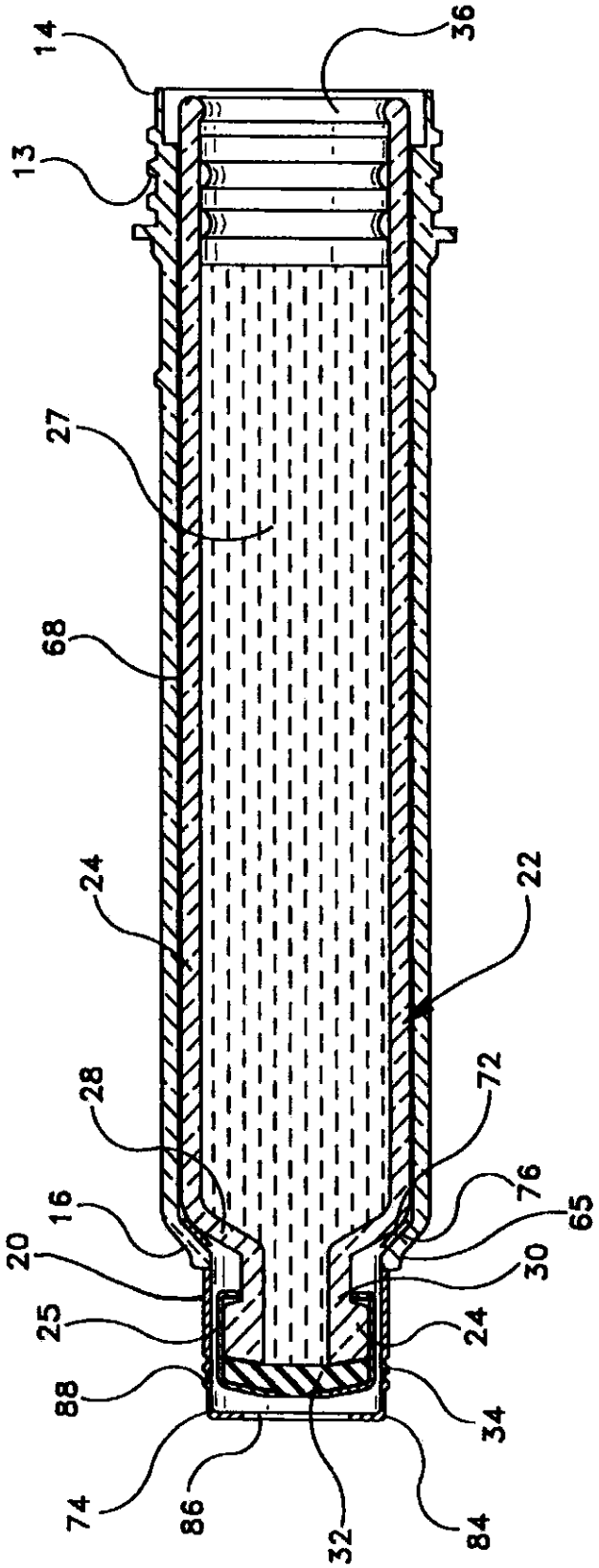


FIG-2

MEDICATION DELIVERY PEN HAVING A 31 GAUGE NEEDLE

BACKGROUND OF THE INVENTION

1. Field of the Invention

The subject invention relates to a medication delivery pen having a 31 gauge needle.

2. Background Description

Medication delivery pens are hypodermic syringes used for self-injection of precisely measured doses of medication. Pens are widely used, for example, by diabetics to dispense insulin.

A typical prior art medication delivery pen includes a cartridge which contains a volume of liquid medication sufficient for several doses. The cartridge includes an elongated generally tubular glass cartridge having a pierceable rubber septum which extends across the open distal end of the cartridge and is securely held in position by a metallic sleeve that is crimped to the distal end of the cartridge. The cartridge also includes a rubber stopper in sliding fluid-tight engagement with interior walls of the cartridge.

Such a medication delivery pen also includes a unitarily molded cartridge retainer having a small diameter tubular neck dimensioned for tightly engaging the neck of the cartridge and the metallic sleeve crimped thereon so as to support and position the entire cartridge. Exterior regions at the extreme distal end of the tubular neck are formed with an array of threads for threadedly receiving the mounting cap of a needle assembly. The medication delivery pen further includes a dosing apparatus that is engaged with the proximal end of the cartridge retainer having a plunger for engaging the rubber stopper of the cartridge. The dosing apparatus includes a dose setting structure used to select the longitudinal distance through which the plunger will move, and dispensing means for driving the plunger the selected distance.

The needle assembly for the medication delivery pen includes an elongate needle cannula having opposed proximal and distal points and a lumen extending therethrough. A plastic cork is adhered to an intermediate position along the needle cannula and in turn is rigidly connected to an end wall of a cylindrical cap. The cylindrical wall of the cap surrounds the proximal point on the needle cannula and includes an array of internal threads for engaging the external threads on the neck of the cartridge retainer.

The medication delivery pen may be used by urging the cap of the needle assembly over the neck of the cartridge retainer sufficiently for the proximal point of the needle cannula to pierce the rubber septum of the cartridge. The cap is then rotated to threadedly engage the neck of the cartridge retainer. The user then manipulates the dosing apparatus to select an appropriate dose. A protective shield over the distal end of the needle cannula is then removed, and the distal point of the needle cannula is injected. The user then actuates the dispensing means of the prior art dosing apparatus to urge the stopper of the cartridge distally and to deliver medication through the lumen of the needle cannula. The needle is then withdrawn, and the needle assembly is separated from the cartridge retainer and safely discarded. The rubber septum of the cartridge reseals itself, and may be pierced again for a subsequent administration of medication. This process may be carried out repeatedly until all of the medication in the cartridge has been used.

A problem with currently available needle assemblies for use on medication delivery pens is the size of the cannula.

Prior to the present invention, 27, 28, 29 and 30 gauge needle cannulas have been commonly used on medication delivery pens, with 30 gauge being the smallest diameter possible. Even though smaller gauges, i.e., 29 and 30 gauge, have helped to reduce pain to patients during injection, there is still a need to provide needle assemblies for medication delivery pens with smaller cannula diameters since small diameter needles are perceived by patients to cause less pain during the injection. However, no one skilled in the art has suggested and no one has provided patients with needle assemblies having a diameter less than 30 gauge.

SUMMARY OF THE INVENTION

The present invention overcomes the 30 gauge limit that has existed for pen needle assemblies by providing a 31 gauge needle assembly for use on medication delivery pens. The 31 gauge needle provides a patient with a needle assembly having a smaller cannula size without loss in performance or structural integrity. The 31 gauge needle assembly mounts on a needle mounting tip of a cartridge retainer assembly on a medication delivery pen and is used like prior art needle assemblies to pierce a patient's arm during an injection process.

However, since the 31 gauge needle cannula is smaller than prior art needle cannulas the penetration force is decreased which reduces the pain caused during an injection procedure. In addition, the smaller cannula size will be seen by the patient prior to the injection so that perceived pain or anticipated pain is also reduced. The reduction in actual and perceived/anticipated pain provided by using the 31 gauge needle on the medication delivery pen is a major benefit to patients that need numerous injections each day, i.e., diabetics requiring insulin injections.

These and other aspects, features and advantages of the present invention will become apparent from the following detailed description taken in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is an exploded perspective view of a medication delivery pen having a needle assembly in accordance with the subject invention; and

FIG. 2 is a cross-sectional view of a cartridge retainer assembly of the medication delivery pen.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

A needle assembly for use on a medication delivery pen **11**, in accordance with the subject invention, is identified generally by the numeral **46** in FIG. **1**. As shown in FIG. I medication delivery pen **11** includes a cartridge retainer assembly **10**, a dosing apparatus **38** and a cartridge assembly **22**. Needle assembly **46**, as described in more detail below, is designed to be attached to a needle mounting insert tip **20** on cartridge retainer assembly **10**.

Cartridge retainer assembly **10**, as shown in FIGS. **1** and **2**, includes an elongate generally tubular body **12** with opposed proximal and distal ends **14** and **16**, respectively. A generally tubular needle mounting insert tip **20** is snap-fit mounted in distal end **16** of body **12** and cartridge retainer assembly **10** is dimensioned and configured to receive a cartridge assembly **22** therein.

Cartridge assembly **22** includes an open proximal end **26** and a distal end **25** defined by an inwardly converging shoulder **28**. A small diameter neck **30** projects distally from

shoulder 28 on cartridge assembly 22, and is provided with a large diameter annular bead 24 extending circumferentially thereabout at the extreme distal end of neck 30. A pierceable and resealable rubber septum 32 extends completely across the open distal end defined by neck 30. Rubber septum 32 is held in place by a metallic sleeve 34 which is crimped around bead 24 at the distal end of neck 30. Medication such as insulin or heparin is pre-filled into cartridge assembly 22 and is retained therein by a rubber stopper 36. Stopper 36 is in sliding fluid-tight engagement with the tubular wall of cartridge assembly 22. Distally directed forces on stopper 36 urge the medication from pen 11 as explained further below.

Dosing apparatus 38 in medication delivery pen 11 is generally cylindrical and includes opposed proximal and distal ends 40 and 42, respectively. Threads 41 are disposed at distal end 42 of dosing apparatus 38 for releasable threaded engagement with proximal end 14 of body 12 of cartridge retainer assembly 10. A plunger rod 44 projects distally from dosing apparatus 38 and is dimensioned to engage stopper 36 of cartridge assembly 22. Dosing apparatus 38 also includes known mechanisms for setting a selected dose of medication to be delivered by pen 11. A dispensing mechanism (not shown) is operative to drive plunger rod 44 a selected distance in a distal direction for moving stopper 36 a distance that will inject the selected dose of medication from cartridge assembly 22. Although a particular prior art dosing apparatus 38 is depicted in FIG. 1, it is to be understood that other dosing apparatus can be used with the needle assembly of the subject invention.

Needle assembly 46, according to the present invention, includes a 31 gauge needle cannula 48 with opposed proximal and distal tips 50 and 52, respectively, and a lumen 51 extending entirely therethrough. The dimensions of 31 gauge needle cannula 48 are set forth below:

Parameter	Value
Outer Diameter	0.010"–0.0105"
Inner Diameter	0.0045"–0.006"
Wall Thickness	0.00225"–0.00275"
Usable length	0.315" (8 mm)
Cannula Material	Stainless Steel

Of course, 31 gauge needle cannulas of other lengths can also be used, i.e., 0.236" (6 mm) or 0.394" (10 mm), and still remain within the scope of the present invention. A cork 54 is securely affixed at an intermediate position along needle cannula 48, and a cap 56 is securely affixed to cork 54. Cap 56 of needle assembly 46 includes an array of internal threads (not shown) for removable mounting needle assembly 46 to needle mounting insert tip 20 on cartridge retainer assembly 10. It is to be understood, however, that other releasable engagement means between needle assembly 46 and cartridge retainer assembly can be provided. For example, external threads can be formed on needle assembly 46 and corresponding internal threads can be defined on cartridge retainer assembly 10 or a bayonet style mounting using lugs and slots can be used. In addition, needle assembly 46 could be "snap fit" on to cartridge retainer assembly 10.

As shown in FIG. 1, body 12 of cartridge retainer assembly 10 includes a plurality of inwardly projecting supports 65 separated from one another by notches 62, wherein supports 65 are used to hold insert tip 20 in distal end 16 of cartridge retainer assembly 10. FIG. 2 is a cross-sectional view of cartridge retainer assembly 10 that shows cartridge assembly 22 within a cartridge receiving chamber 68. FIGS. 1 and 2 also show an array of threads 13 on proximal end 14 of body 12 used to engage threads 41 on distal end 42 of dosing apparatus 38.

Needle mounting insert tip 20 of cartridge retainer assembly 10 includes opposed proximal and distal ends 72 and 74, respectively. As shown in FIG. 2, proximal end 72 of needle mounting insert tip 20 includes a rim 76 extending therefrom that is diametrically dimensioned to closely engage metallic sleeve 34 crimped to cartridge assembly 22 for holding rubber septum 32 in place. Distal end 74 of needle mounting insert tip 20 includes a generally annular end wall 84 having an aperture 86 extending therethrough for access by proximal point 50 of needle cannula 48. An array of outwardly disposed threads 88 is defined intermediate proximal and distal ends 72 and 74, respectively. Threads 88 are disposed and dimensioned for engaging threads on needle assembly 46.

Assembly of medication delivery pen 11 is performed by inserting cartridge assembly 22 into cartridge retainer assembly 10. More particularly, neck 30 and crimped metallic sleeve 34 of cartridge assembly 22 are inserted in a proximal to distal direction into open proximal end 14 of body 12 of cartridge retainer assembly 10. Crimped metallic sleeve 34 eventually will pass entirely through body 12, and further advancement of cartridge assembly 22 into cartridge retainer assembly 10 will require entry of crimped metallic sleeve 34 into rim 76 extending from proximal end 72 of needle mounting insert tip 20. Considerable dimensional variation and eccentricities between the neck and body of prior art cartridges are known to exist. If such eccentricities do exist, crimped metallic sleeve 34 will rest on rim 76 of insert tip 20 to center sleeve 34 relative to body 12 into a position that conforms with any dimensional inconsistencies or eccentricities in cartridge assembly 22.

Further distally directed movement of cartridge assembly 22 into cartridge retainer assembly 10 will cause shoulder 28 of cartridge assembly 22 to seat against rim 76 of insert tip 20. Rim 76 therefore defines the fully seated position of cartridge assembly 22 in cartridge retainer assembly 10 and functions to securely engage cartridge assembly 22. In this fully seated position, as shown most clearly in FIG. 2, septum 32 of cartridge assembly 22 is spaced proximally from distal wall 84 of needle mounting insert tip 20. Dosing apparatus 38 is then assembled to proximal end 14 of the body of cartridge retainer assembly 10 such that plunger rod 44 of dosing apparatus 38 engages stopper 26 of cartridge assembly 22.

Medication delivery pen 11 is used by mounting needle assembly 46 to needle mounting insert tip 20 of cartridge retainer assembly 10. This mounting is achieved by moving needle assembly 46 in a proximal direction over needle mounting insert tip 20 until the threads (not shown) of cap 56 engage external threads 88 on needle mounting insert tip 20. Threads 88 of needle mounting insert tip 20 are spaced from the extreme distal end of needle mounting insert tip 20, therefore, the initial axial advancement of cap 56 over needle mounting insert tip 20 will cause proximal point 50 of needle cannula 48 to pierce rubber septum 32 of cartridge assembly 22 prior to rotational threaded engagement of needle assembly 46 with needle mounting insert tip 20. Thus, the bevel which defines proximal point 50 will advance axially through septum 32 without a rotation that could tear rubber septum 32.

After threads of cap 56 engage threads 88 of needle mounting insert tip 20, further advancement of needle

assembly **46** requires relative rotation between cap **56** and needle mounting insert tip **20**. It will be appreciated that needle mounting insert tip **20** is too small to be readily griped by the user of medication delivery pen **11**, and is partly covered by cap **56**. However, the relative rotation can be achieved by rotating body **12** of cartridge retainer assembly **10**. Since needle mounting insert tip **20** is locked to distal end **16** on body **12** of cartridge retainer assembly **10**, rotation of body **12** is transmitted to needle mounting insert tip **20** and enables complete rotational engagement of needle assembly **46**.

Use of medication delivery pen **11** proceeds in a conventional manner with dosing apparatus **38**. Actuation of dosing apparatus **38** causes liquid medication in cartridge assembly **22** to be urged in a distal direction through lumen **51** of needle cannula **48**. This distally directed liquid pressure also will cause septum **32** to distend in a distal direction. However, as noted above and as shown in FIG. **2**, septum **32** is spaced proximally from cork **54** of needle assembly **46**, and will not be urged into contact with cork **54**. Thus, drooling or weeping of liquid medication can be substantially prevented. This is enabled because cartridge assembly **22** is supported and accurately positioned by engagement of cartridge shoulder **28** with rim **76** on insert tip **20**. Hence neck **30** and crimped metallic sleeve **34** need not be closely engaged by needle mounting insert tip **20**. After medication delivery pen **11** has been used, needle assembly **46** is separated from needle mounting insert tip **20** and discarded.

In the foregoing discussion, it is to be understood that the above-described embodiments of the present invention are simply illustrative of various features of a cartridge retainer assembly for a medication delivery pen. Other suitable variations, modifications and combinations of these features could be made to or used in these embodiments and still remain within the scope of the present invention.

What is claimed is:

1. A medication delivery pen for delivering medication to a patient during an injection procedure comprising:

a needle assembly having a 31 gauge needle cannula;

a cartridge assembly containing medication having a proximal and distal end, said proximal end including an array of threads and a stopper and said distal end including means for attaching said needle assembly so that medication can flow through said 31 gauge needle cannula during an injection procedure; and

a dosing apparatus having opposed proximal and distal ends with an array of threads at said distal end for threaded engagement with said threads at said proximal end of said cartridge assembly, said dosing apparatus further comprising a plunger rod projecting beyond said distal end of said dosing apparatus for selective engagement with said stopper in said cartridge assembly, and means for moving said plunger rod distally in said dosing apparatus selected amounts, whereby said plunger rod moves said stopper in said cartridge assembly to dispense medication from said cartridge assembly through said 31 gauge needle cannula.

2. A medication delivery pen according to claim **1**, wherein said 31 gauge needle cannula has an outer diameter less than 0.0105 inches.

3. A medication delivery pen according to claim **1**, wherein said 31 gauge needle cannula has an outer diameter no smaller than 0.010 inches and no larger than 0.0105 inches.

4. A medication delivery pen according to claim **1**, wherein said 31 gauge needle cannula has an inner diameter no smaller than 0.0045 inches and no larger than 0.006 inches.

5. A medication delivery pen according to claim **1**, wherein said 31 gauge needle cannula is made of stainless steel.

6. A medication delivery pen according to claim **1**, wherein said 31 gauge needle cannula has a usable length of approximately 0.315 inches.

7. A medication delivery pen according to claim **1**, wherein said 31 gauge needle cannula has a usable length of approximately 0.236 inches.

8. A medication delivery pen according to claim **1**, wherein said 31 gauge needle cannula has a usable length of approximately 0.394 inches.

9. A medication delivery pen according to claim **1**, wherein said 31 gauge needle cannula has a wall thickness no smaller than 0.00225 inches and no larger than 0.00275 inches.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,146,361
DATED : November 14, 2000
INVENTOR(S) : Michael A. Dibiasi et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title page,
Item [56], **References Cited,** FOREIGN PATENT DOCUMENTS, insert
-- 279583B1 10/1993 European Pat. Off. --.
OTHER PUBLICATIONS, after "Novo Nordisk A/S":"Red Cassel" should read
-- Fred Cassel --.
Item [75], Inventors, "**Michael D. DiBiasi**" should read -- **Michael A. DiBiasi** --.

Column 3,
Line 50, "cap 56" should read -- cap or hub 56 --;
Line 52, "removable" should read -- removably --;
Line 56, "assembly" should read -- assembly 10 --.

Column 5,
Line 4, "griped" should read -- gripped --.

Column 6,
Line 42, insert
-- 10. An insulin injection system comprising a pen shaped syringe comprising a cartridge with insulin and an injection needle, wherein the needle is a 31 gauge needle and the cartridge contains an insulin type that may freely flow through a 31 gauge needle.

11. An insulin injection system according to Claim 10, wherein the pen shaped syringe is designed to receive cartridges containing insulin which may pass freely through a 31 gauge needle.

12. An insulin injection system according to Claim 10, wherein the needle has attaching means for cooperation with attaching means on the pen shaped syringe.

13. An insulin injection system according to Claim 12, wherein the needle attaching means is a needle hub having a thread cooperating with a corresponding thread on the pen shaped syringe.

14. An insulin injection system according to Claim 13, wherein the needle hub has a central protrusion covering part of the length of the needle.

15. An insulin injection system according to Claim 14, wherein the length of the injection part of the needle is 8mm.

16. An insulin injection system according to Claim 14, wherein the length of the injection part of the needle is 10mm.

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,146,361
DATED : November 14, 2000
INVENTOR(S) : Michael A. Dibiasi et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

17. A needle assembly comprising:

(a) a needle hub having a base and a needle fitting for removably mounting said needle assembly on a pen-type insulin syringe having a mounting and which accepts cartridges containing insulin that may flow freely through a 31 gauge needle; and

(b) a 31 gauge needle secured in said base and having first and second needle portions extending from said base in opposite directions.

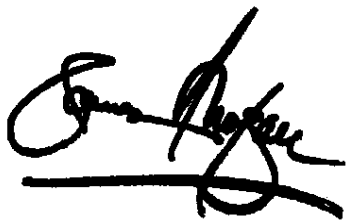
18. A needle assembly according to Claim 17, wherein said needle fitting includes an annular sleeve extending from said base such that said sleeve surrounds said first needle portion concentrically and is spaced therefrom, and wherein said sleeve has a threaded interior by which it may be screwed onto an externally threaded hub-receiving part of a pen-type insulin syringe.

19. A needle assembly according to Claim 18, wherein said second needle portion has a predetermined length appropriate for injecting insulin into a human patient.

20. A needle assembly according to Claim 19, wherein said base further comprises a central protrusion which extends from said base for a predetermined distance along said second needle portion and embeds said second needle portion along the said distance, and wherein said second needle portion further comprises an exposed end which projects axially from said central protrusion and which has a length corresponding to the desired depth of needle insertion into a human patient. --

Signed and Sealed this

Seventeenth Day of December, 2002



JAMES E. ROGAN
Director of the United States Patent and Trademark Office

EXHIBIT 14

United States Patent [19]

Sams

[11] **Patent Number: 4,936,833**

[45] **Date of Patent: Jun. 26, 1990**

[54] **CARTRIDGE-HOLDER ASSEMBLY FOR MEDICATION DISPENSING UNIT**

[75] Inventor: **Bernard Sams, London, England**

[73] Assignee: **Hypoguard (UK) Limited, Woodbridge, England**

[21] Appl. No.: **237,147**

[22] Filed: **Aug. 26, 1988**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 205,198, Jun. 10, 1988, Pat. No. 4,865,591, which is a continuation-in-part of Ser. No. 81,241, Aug. 4, 1987, abandoned.

[51] **Int. Cl.**[5] **A61M 5/24**

[52] **U.S. Cl.** **604/232; 604/208; 604/209; 604/220; 222/391**

[58] **Field of Search** 604/68, 72, 208–210, 604/218, 220, 232, 234, 197; 222/325, 340, 391

[56] **References Cited**

U.S. PATENT DOCUMENTS

2,646,798	7/1953	Brown	604/232 X
3,110,309	11/1963	Higgins	604/201
3,930,499	1/1976	Rimbaud	604/197
3,976,069	8/1976	Ong	604/232 X
4,573,973	3/1986	Mezi	604/197
4,592,745	6/1986	Rex	604/211

FOREIGN PATENT DOCUMENTS

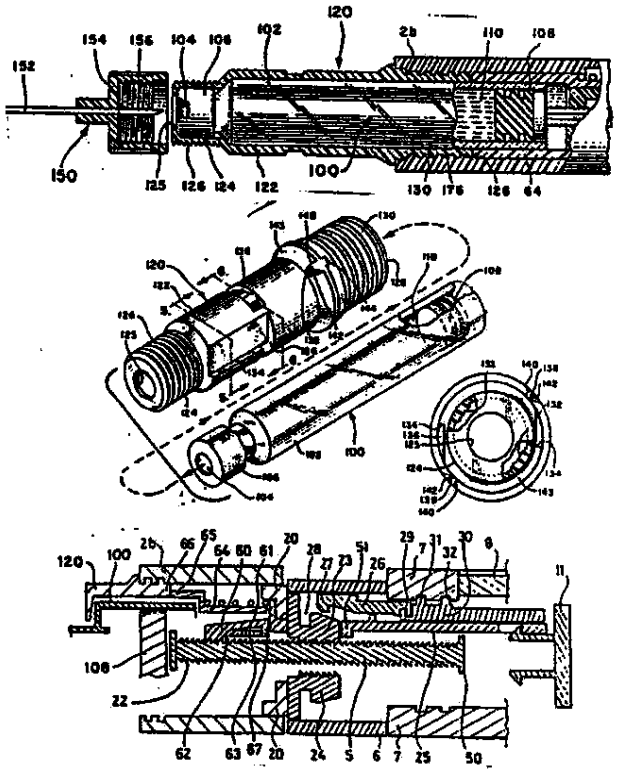
22140	10/1961	German Democratic Rep.	222/391

Primary Examiner—Martin P. Schwadron
Assistant Examiner—Allen J. Flanigan
Attorney, Agent, or Firm—Willian Brinks Olds Hofer Gilson & Lione

[57] **ABSTRACT**

A cartridge assembly for a syringe-type medication dispensing unit includes a cartridge having a cartridge body with first and second ends. A pierceable membrane is mounted at the first end and a piston is mounted at the second end, with a volume of medication contained in the cartridge body between the membrane and the piston. A cartridge holder receives the cartridge and defines first and second ends. The first holder end defines a central opening and an external thread for mounting a double-ended needle. The second holder end defines an external thread for securing the holder to a medication dispensing unit and an actuating shoulder. The holder frictionally engages the cartridge to form an assembly which can be handled as a single modular unit with the cartridge held securely in the holder by frictional engagement.

23 Claims, 6 Drawing Sheets



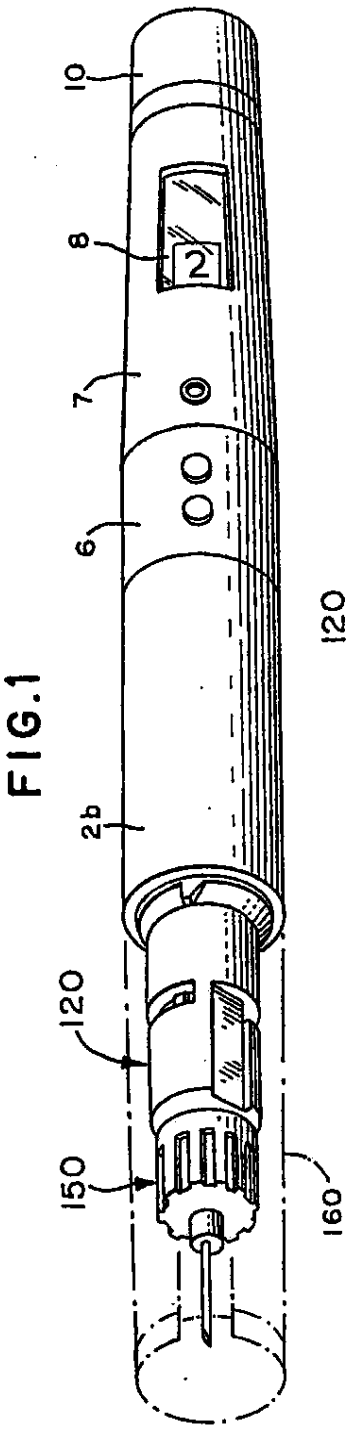

10
8
2
7
6
2b
120
150
160

FIG. 1

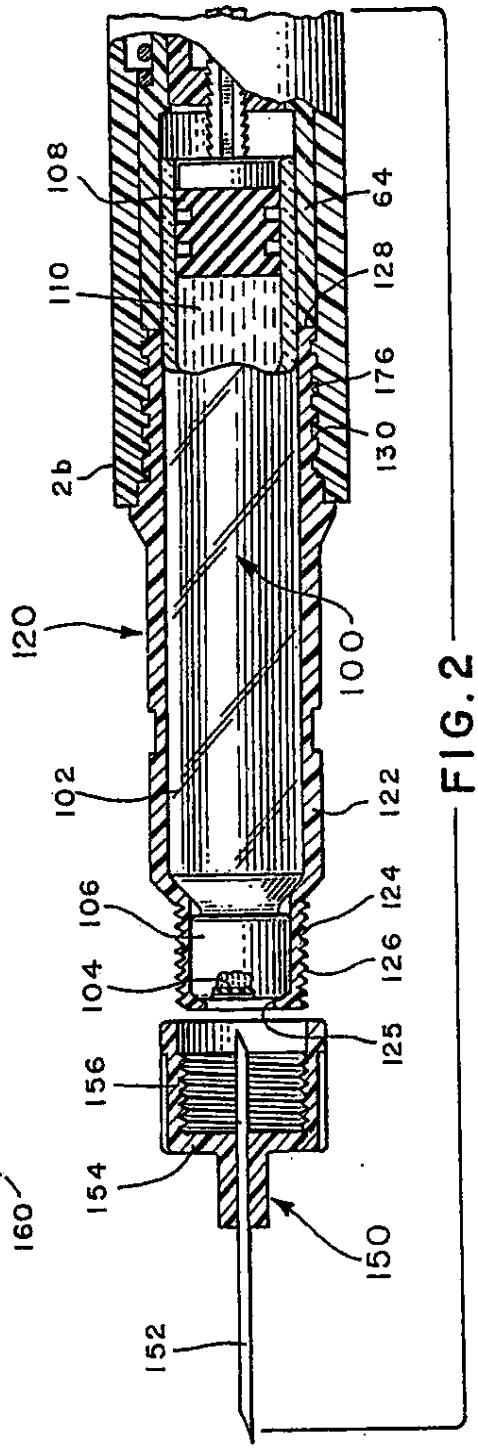

108
64
110
128
176
130
2b
120
100
102
122
106
124
104
126
125
156
154
150
152

FIG. 2

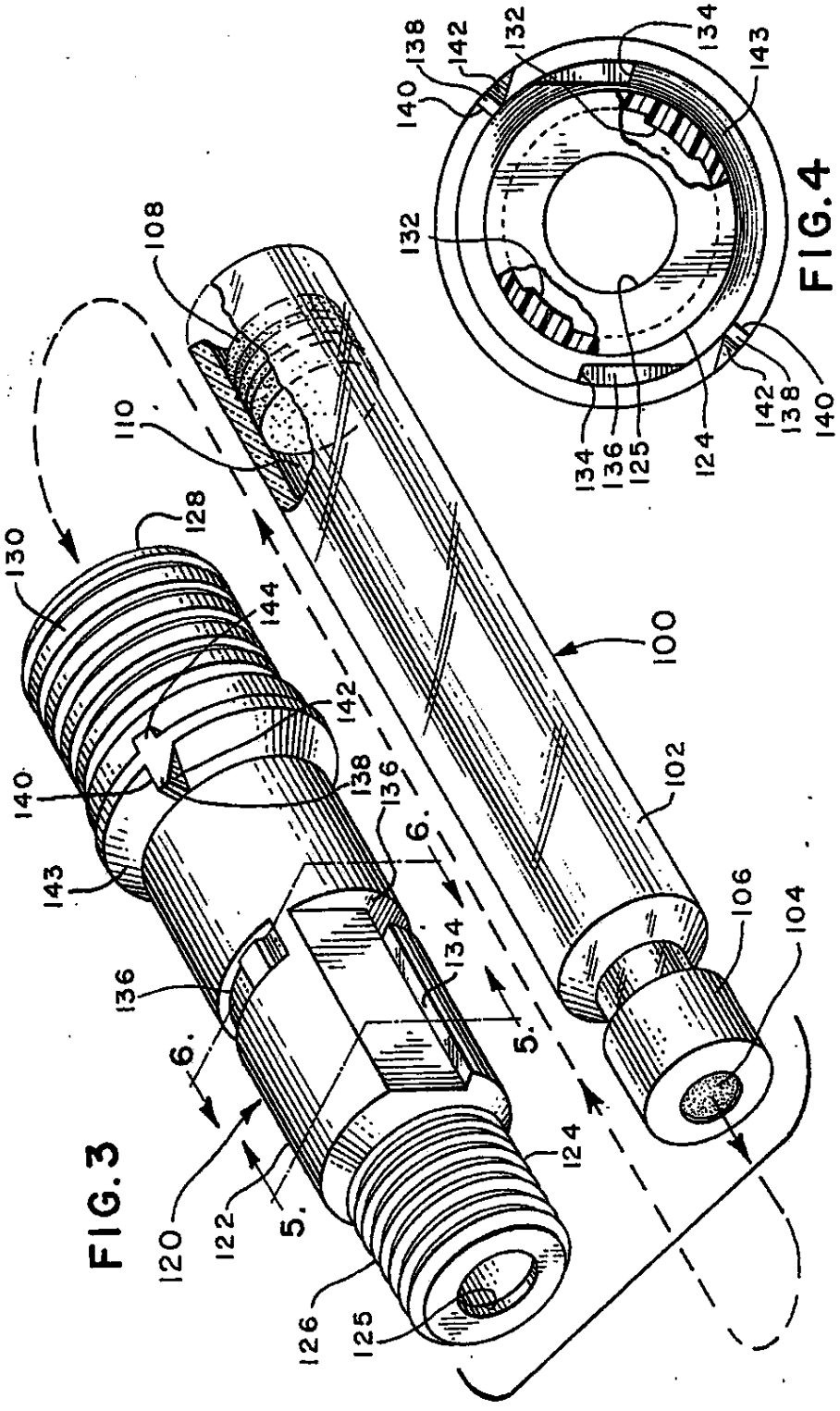

108
110
128
130
144
142
140
138
136
143
134
6.
5.
100
102
106
104
124
120
122
126
125

FIG. 3

138
142
132
134
143
140
132
134
136
125
124
142
138
140

FIG. 4

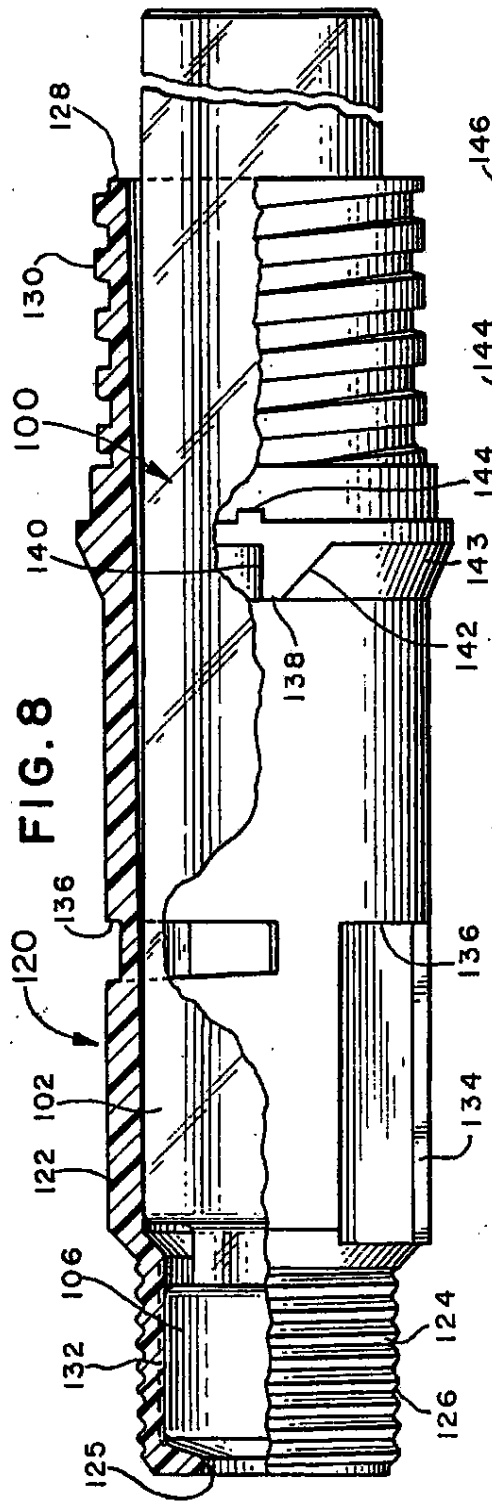


FIG. 8

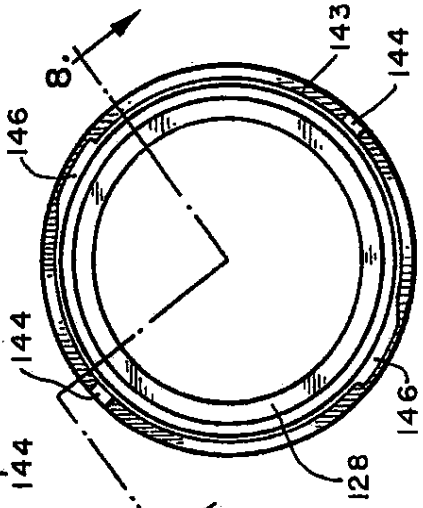


FIG. 7

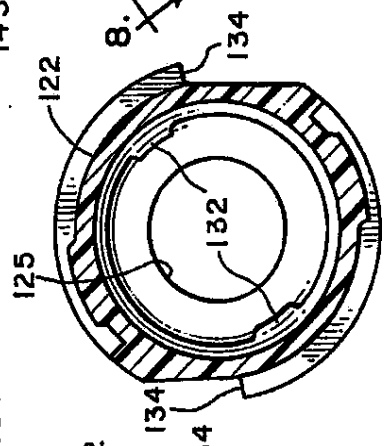


FIG. 6

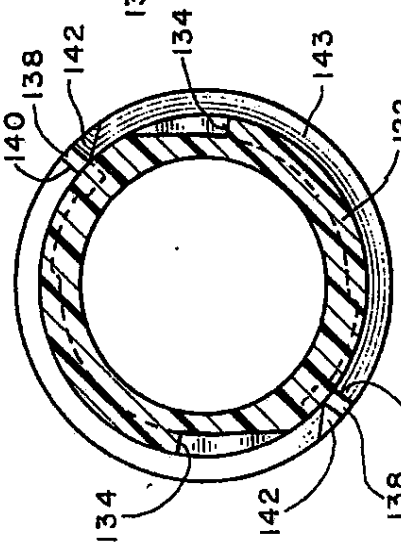


FIG. 5

FIG.9

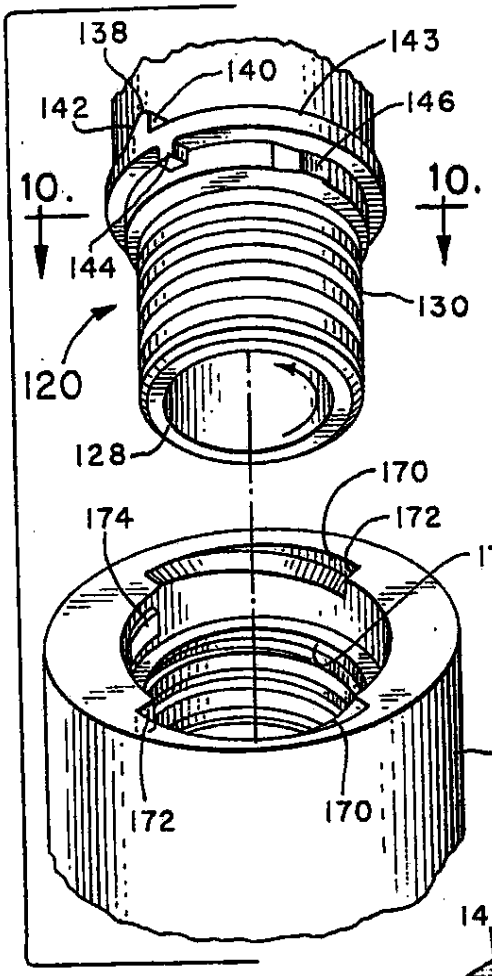
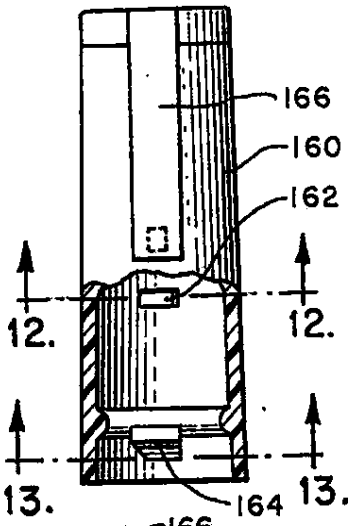


FIG.11



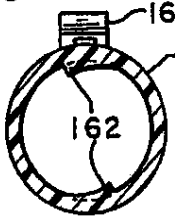


FIG.12

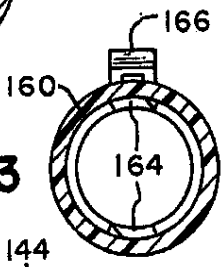


FIG.13

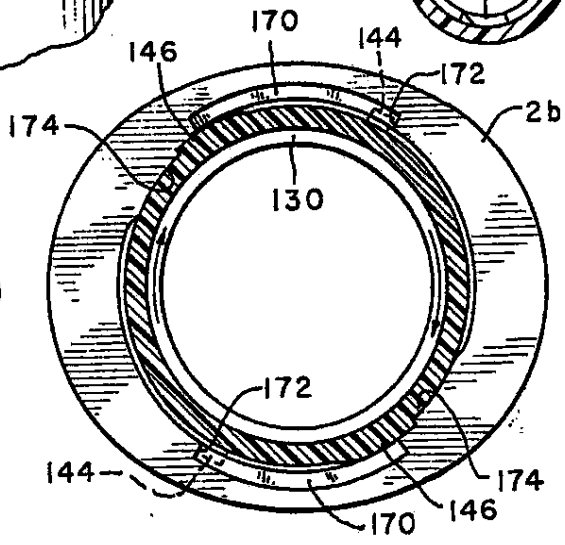


FIG.10

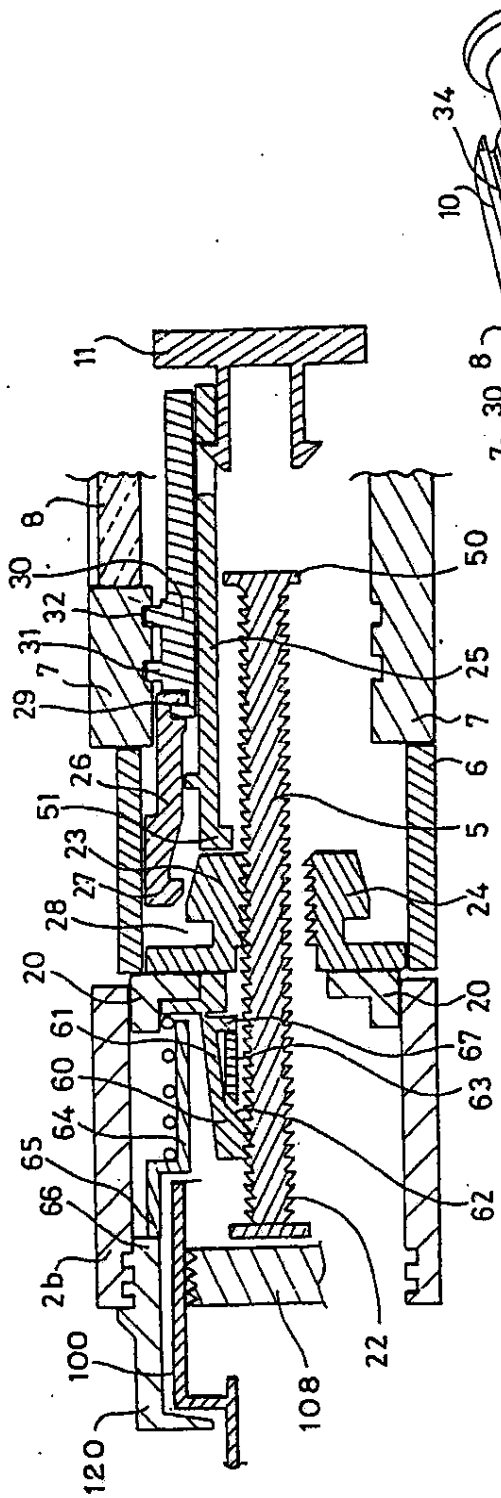

11
8
30
32
31
7
29
26
51
23
27
28
20
61
60
64
65
66
2b
100
120
108
22
50
25
7
6
5
24
20
67
63
62

FIG. 14

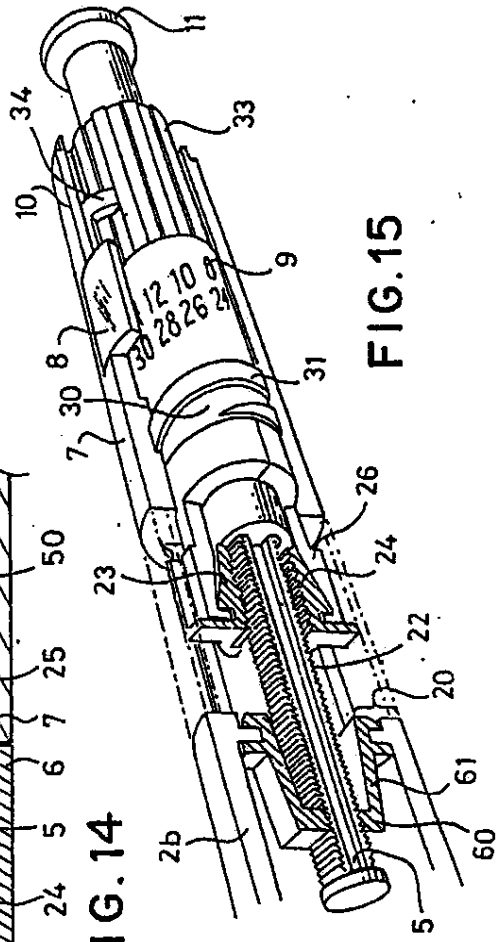

11
34
33
10
9
12 10 6
30 28 26 24
8
31
30
7
26
24
23
22
20
61
60
2b
5

FIG. 15

CARTRIDGE-HOLDER ASSEMBLY FOR MEDICATION DISPENSING UNIT

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of copending U.S. patent application Ser. No. 07/205,198, filed Jun. 10, 1988, now U.S. Pat. No. 4,865,591, which is in turn a continuation-in-part of U.S. patent application Ser. No. 07/081,241, filed Aug. 4, 1987, now abandoned. The entire text of these applications Ser. Nos. 07/205.198 and 07/081,241 is hereby incorporated by reference.

BACKGROUND OF THE INVENTION

The present invention relates to a cartridgeholder assembly for a measured dose medication dispensing device.

Patients suffering from diabetes often have to inject themselves with frequent doses of insulin and this can be done using a conventional syringe. However, such patients often also suffer from side effects of their illness and are not capable of accurately controlling the operation of such a syringe. It is therefore desirable that they should be provided with means for automatically administering an accurately controlled dosage. The dosage required by different patients can vary over quite wide ranges, from for example 2 units of insulin per dose to 30 or more units, and it is necessary to ensure that any device is capable of selecting a range of dosages simply and accurately.

Dispensing devices such as that shown in Rex U.S. Pat. No. 4,592,745 utilize a cartridge having a pierceable membrane at one end and a movable piston at the other, with a volume of a medication such as an insulin solution contained therebetween. The cartridge is mounted in a dispensing device which includes a plunger, a one-way mechanism that permits the plunger only to advance, and a mechanism for advancing the plunger to dispense medication.

The device disclosed in the Rex patent utilizes the rear rim of the cartridge to actuate the one-way mechanism: when the cartridge is removed the one-way mechanism releases, allowing the plunger to retract, but when the dispensing device is assembled with the cartridge in place the rear rim of the cartridge causes the one-way mechanism to engage the plunger. The cartridge is received loosely in a section of the device, and the one-way mechanism engaging apparatus resiliently holds the cartridge in position.

The dispensing device of the Rex patent has been proven effective and reliable in use. Nonetheless, it suffers from certain disadvantages related to the fact that the walls of the cartridge are formed of glass and in commercially practical cartridges it is difficult to control the overall length of the cartridge accurately. Resulting variations in the length of the cartridge cause the one-way mechanism to be engaged at a variable position as the cartridge enclosing section is screwed into place in the dispensing unit. If the cartridge is unusually long, the one-way mechanism will be engaged well before the cartridge enclosing section reaches its final position, and the plunger will then pressurize the contents of the cartridge as the section is screwed home. Such pressurization will produce a squirt of medication when the needle pierces the membrane. Some users may object to this unintended release of medication.

The variable length of the cartridge also imposes design constraints on the Rex dispensing device. As mentioned above, the cartridge fits loosely within the cartridge receiving section, and the cartridge is held in position by forces applied to the rear rim of the cartridge by the engaging apparatus for the one-way mechanism discussed above. This engaging apparatus must provide resilient support to the rim over the full range of cartridge lengths. Otherwise, the cartridge may be subjected to excessive axial forces, or it may alternately be left free to move axially in the dispensing device. The resilient mounting of the engaging apparatus in no way overcomes the problems discussed above related to unintended pressurization of the cartridge.

The present invention is directed to an improved cartridge-holder assembly that overcomes these prior art problems.

SUMMARY OF THE INVENTION

According to this invention, a cartridgeholder assembly is provided for a syringe-type medication dispensing unit. The cartridge comprises a cartridge body having first and second ends, a pierceable membrane mounted at the first end, and a piston mounted at the second end, with a volume of medication contained in the cartridge body between the membrane and the piston. The holder defines a first holder end which defines a central opening and means for mounting a double ended needle. The second holder end defines means for securing the holder to a medication dispensing unit and an actuating shoulder. The holder defines a central cavity shaped to receive and frictionally engage the cartridge to form an assembly that can be handled as a single, modular unit with the cartridge held frictionally in the holder.

This arrangement overcomes the prior art problems discussed above. The holder can easily be manufactured to high precision, and the actuating shoulder can therefore be accurately positioned to actuate the one-way mechanism just as the holder reaches its fully assembled position on the dispensing device. This substantially eliminates the problem of unintended pressurization of the cartridge before the needle is inserted into the membrane. Secondly, the releasable engagement between the cartridge and the holder allows the cartridge to be held in place without engagement of the rim. This relaxes design constraints on the engaging apparatus for the one-way mechanism.

As yet another advantage, the modular assembly of the holder and cartridge can be handled and assembled onto the dispensing device as a unit. This simplifies assembly by the patient.

The housing is preferably formed from a clear plastic material, and a user can therefore readily observe the movement of the piston within the cartridge and can assess the amount of medication in the cartridge. The housing also provides a measure of protection to the cartridge, both physical and against pathogenic organisms and other possible contamination.

The needle end of the cartridge can project through a terminal aperture in the housing or that end of the housing can be closed and can carry a needle or other outlet integrally therewith which projects axially inwardly into the housing to penetrate the membrane at the end of the cartridge.

The cartridge houses the piston which is to be moved by the plunger of the dispensing device. This piston can

be of conventional design and will usually form part of the cartridge as commercially available. The plunger acts on the piston and the piston can carry a socket or other recess to receive and locate the head of the plunger. In some cases, the plunger can be affixed to the piston and will form part of the cartridge as supplied, in which case the plunger will extend into the device when the cartridge is mounted on the device. However, it is preferred that the plunger form part of the device rather than of the cartridge and, for convenience the invention will hereinafter be described with respect to this configuration.

The invention itself, together with further objects and attendant advantages, will best be understood by reference to the following detailed description. taken in conjunction with the accompanying drawings

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a perspective view of a syringe-type medication dispensing unit which includes a preferred embodiment of the cartridge-holder assembly of this invention.

FIG. 2 is a partial view of portions of the unit of FIG. 1 in partial section.

FIG. 3 is an exploded perspective view of the cartridge-holder assembly of FIG. 1.

FIG. 4 is a front view in partial cutaway of the holder of FIG. 3.

FIG. 5 is a cross sectional view taken along line 5—5 of FIG. 3.

FIG. 6 is a cross sectional view taken along line 6—6 of FIG. 3.

FIG. 7 is a rear view of the holder of FIG. 3.

FIG. 8 is a longitudinal sectional view taken along line 8—8 of FIG. 7 in partial elevation.

FIG. 9 is an exploded perspective view of portions of the dispensing device of FIG. 1.

FIG. 10 is a sectional view taken along line 10—10 of FIG. 9.

FIG. 11 is an elevational view in partial cutaway of the cap of FIG. 1.

FIG. 12 is a cross sectional view taken along line 12—12 of FIG. 11.

FIG. 13 is a cross sectional view taken along line 13—13 of FIG. 11.

FIG. 14 is a schematic cross sectional view of portions of the dispensing device of FIG. 1.

FIG. 15 is a perspective view in partial cutaway of portions of the dispensing device of FIG. 1.

DETAILED DESCRIPTION OF THE PRESENTLY PREFERRED EMBODIMENTS

FIGS. 1-10 show various views of the preferred embodiment of the cartridge-holder assembly of this invention, and FIGS. 11-15 provide further details relating to a preferred dispensing unit suitable for use with the cartridge-holder assembly of FIGS. 1-10.

Turning now to FIGS. 1-10, the preferred embodiment of the assembly of this invention comprises a cartridge 100 and a cartridge holder 120. FIG. 1 shows the holder 120 mounted to a dispensing device, and FIG. 2 shows the cartridge 100 mounted within the holder 120. As best shown in FIGS. 2 and 3, the cartridge 100 includes a generally cylindrical body 102 which is closed at one end by a pierceable membrane 104 and is sealed at the other end by a movable piston 108. A medication such as an insulin solution 110 is contained within the body 102 between the membrane 104 and the piston 108. In the conventional manner, a collar 106 of metal surrounds the membrane 104 and secures the membrane 104 to the body 102 in a fluid-tight manner.

The cartridge 100 can be quite similar to conventional glass cartridges. Of course, the dimensions of the cartridge should be chosen to match the dispensing device. Preferably, the body 102 is glass coated with silicone to reduce friction with the piston. The piston 108 is preferably about two-thirds the axial length of conventional pistons, also to reduce friction.

As best shown in FIGS. 2 and 8, the cartridge holder 120 comprises a tubular element 122 which defines a narrowed neck 124 which terminates in a central opening 125. External threads 126 are formed around the exterior of the neck 124. The opposite end of the cartridge holder 120 defines an annular actuating shoulder 128 positioned adjacent to a second set of external threads 130. The tubular element 122 is sized to receive the cartridge 100 and defines in this embodiment two axially oriented raised lands 132 which are positioned to frictionally engage the collar 106 of the cartridge 100.

The exterior of the tubular element 122 defines a number of features which cooperate with other components of the dispensing device described below. In particular, the tubular element 122 defines a pair of axial grooves 134 which communicate with respective circumferential grooves 136 to form L-shaped grooves that form part of a bayonet mount as described below. The tubular element 122 also defines a pair of stop members 138 which cooperate with a cap as described below. Each of the stop members 138 defines a transverse face 140 and an opposed sloping face 142. The tubular element 122 also defines an annular flange 143 which in turn defines two rearwardly extending stop members 144. A pair of ramps 146 are defined on the exterior of the tubular member 122 near the external threads 130.

Preferably, the cartridge holder 120 is formed of a transparent plastic material such as polycarbonate. This construction allows a user to see the cartridge 100 within the cartridge holder 120 to check the correct insulin and to gauge the amount of medication 110 left in the cartridge 100.

The minimum diameter of the inside of the tubular element 122 is greater than the maximum diameter of the cartridge 100. For this reason, the tubular element 122 receives the cartridge 100 in an easy sliding fit such that the weight of the cartridge 100 will move the cartridge 100 in the tube 122 until the collar 106 contacts the raised lands 132. A slight additional force will push the cartridge 100 to the fully seated position shown in FIG. 8. In this position friction between the lands 132 and the collar 106 will prevent the cartridge 100 from falling out of the holder 120. This arrangement facilitates assembly of the cartridge 100 into the holder 120, because no frictional retarding force is encountered until the cartridge 100 is almost in the fully assembled position. There is therefore, less chance that a user will fail to push the cartridge 100 fully into the holder 120. Furthermore because the cartridge 100 is engaged at the collar 106, it is the diameter of the collar 106 rather than the diameter of the tube 122 that determines the tightness of the friction fit. In many cases, the diameter of the collar 106 can be controlled more closely than the diameter of the glass tube 122, and in these cases this arrangement provides the further advantage of a more consistent fit.

Thus, the lands 132 frictionally engage the collar 106 to releaseably hold the cartridge 100 in the holder 120

and thereby to form a modular unit which can be handled and assembled as a single device. As apparent in FIGS. 2 and 8, the end of the cartridge 100 that mounts the piston 108 extends out of the cartridge holder 120 for a considerable distance. In this embodiment, that distance is greater than one-half inch. This allows the user to grasp the cartridge 100 when it is necessary to remove the cartridge 100 from the cartridge holder 120 for replacement.

As shown in FIG. 2, the external threads 126 are sized to mate with internal threads 156 defined by a needle assembly 150. This needle assembly 150 includes a double-ended hypodermic needle 152 which is mounted to a hub 154 that in turn defines the internal threads 156. By threading the needle assembly 150 onto the external threads 126 the needle 152 is passed through the central opening 125 and the membrane 104, into contact with the medication 110.

As shown in FIGS. 1 and 11–13 the dispensing device includes a removable cap 160 which, when mounted in position, surrounds and protects the needle assembly 150 (if mounted), the cartridge holder 120, and the cartridge 100. This cap 160 defines a pair of internal lugs 162 sized to fit within the grooves 134, 136 to form a bayonet mount in order to hold the cap 160 securely in position on the cartridge holder 120. In addition, the cap 160 defines a pair of protruding elements 164 positioned to interact with the stop members 138. When the cap 160 is rotated in a first locking direction, the protruding elements 164 engage the transverse faces 140, thereby defining a stop position. This allows the cap 160 to be used as a tool to apply torque to screw the cartridge holder 120 into place on the dispensing device without overtightening the bayonet mount. When the cap 160 is rotated in a second unlocking direction, the protruding elements engage the sloping faces 140 to shift the cap 160 axially. The cap 160 can if desired define a clip 166 to retain the dispensing device in a pocket of the user.

As shown in FIGS. 2 and 9 the cartridge holder 120 mounts in the dispensing device by screwing the external threads 130 into a collar 2*b* defined by the dispensing device. This collar 2*b* defines internal threads 176 which mate with the external threads 130. In addition the collar 2*b* defines elements which cooperate with the stop members 144 and the ramps 146 to define the fully assembled position of the cartridge holder 120 and to hold it in that position. In particular, the collar 2*b* defines a pair of spiral grooves 170, each of which terminates in a transverse face 172. When the cartridge holder 120 is threaded into the collar 2*b* the stop members 144 enter the spiral grooves 170. The faces 172 prevent overtightening of the cartridge holder 120 in the collar 2*b*. The collar 2*b* defines ramps 174 which cooperate with the ramps 146 to define a detent that tends to hold the cartridge holder 120 in the fully assembled position (FIG. 10).

As best shown in FIG. 2, when the cartridge holder 120 is assembled in the collar 2*b* the rear end of the cartridge 100 is unrestrained. This arrangement provides particular advantages, because the overall length of the cartridge 100 is difficult to control with conventional manufacturing processes, as explained above. This embodiment accommodates varying lengths of the cartridge 100 because the rear rim of the cartridge body 102 does not contact the dispensing unit. In order to prevent the cartridge 100 from moving undesirably after the cartridge holder 120 has been threaded into the collar 2*b*, the cartridge 100 is restrained from movement by the frictional fit with the raised lands 132 described above.

As described in greater detail below, the dispensing device includes a plunger 5 that is advanced against the piston 108 to dispense the medication 110 through the needle 152.

The movement of this plunger 5 is controlled in part by a one-way mechanism that allows the plunger 5 to advance but not to retract as long as the cartridge holder 120 is mounted to the collar 2*b*. However, when the cartridge holder 120 is removed from the collar 2*b* to replace the cartridge 100, this one-way mechanism is released, to allow the plunger 5 to be retracted into the dispensing unit. The details of operation of this one-way mechanism and the manner in which this mechanism is released are explained in detail below in conjunction with FIGS. 14 and 15. Here, it is enough to note that the one-way mechanism is controlled by the axial position of a member 64 which is slidably mounted in the collar 2*b*. This member 64 abuts the actuating shoulder 128 of the cartridge holder 120 and is shifted rearwardly to engage the one-way mechanism with the plunger 5 when the cartridge holder 120 is mounted in place in the collar 2*b*.

It is the actuating shoulder 128 rather than any part of the cartridge 100 that determines the position of the one-way mechanism actuating member 64. The cartridge holder 120 can readily be manufactured to high accuracy with conventional molding techniques, and for this reason the actuating shoulder 128 can be precisely positioned to ensure that the member 64 is depressed at the proper instant, just before the cartridge holder 120 is fully assembled into the collar 2*b*. This ensures that there is no substantial movement of the cartridge holder 120 or the cartridge 100 after the one-way mechanism is engaged. This prevents the plunger 5 from exerting undue forces on the piston 108 and minimizes the unintended discharge of medication 110 when the needle 152 pierces the membrane 104.

Further details of the one-way mechanism, and the operation of the actuating member 64, as well as the advancing mechanism for the plunger 5 will now be described in conjunction with FIGS. 14 and 15.

As shown in highly schematic form in FIG. 14 and as discussed above, the cartridge 100 is housed in the housing 120 which is screw fit into the collar 2*b* extending axially from the front end of the dispensing unit.

The dispensing device is provided with a pawl type one-way mechanism which engages teeth on the plunger 5 so as to prevent rearward movement of the plunger 5 once the housing 120 is in place. This one-way mechanism is shown at 60 in FIGS. 14 and 15 and is biassed to retract radially when the cartridge housing 120 is removed. For example, the housing can incorporate a twist mechanism which both locks the cartridge housing in position and actuates the one-way mechanism; or the shoulder 128 of the cartridge housing 120 can bear against part of the one-way mechanism as it seats home to actuate the one-way mechanism. The one-way mechanism disengages when the cartridge housing 120 is removed to allow the plunger 5 to be retracted into the device to permit a new cartridge 100 to be mounted on the dispensing device.

A preferred form of the one-way mechanism is shown in FIG. 14 and comprises a pair of diametrically opposed pawls 60 carried on spring arms 61 snap fitted onto an annular shoulder 20 to extend forward of the

shoulder into the axial socket in which the cartridge 100 is received. The pawls 60 have an inclined rearward face 62 which bears against a correspondingly angled face carried by a collet 63 mounted around the plunger shank and radially inward of arms 61. The collet is attached to a spring loaded sleeve 64 which is a slideable fit within the socket and is spring biassed into its forward position. The front end of the sleeve 64 provides a stop 65 against which the shoulder 128 of the housing 120 bears as it is mounted in the device. This causes the sleeve 64 to be moved axially rearwardly to carry the inclined face of collet 63 clear of the inclined face 62 of the pawl and to bring the rear edge of collet 63 into contact with a stop 67 carried on the radially inward face of arm 61. This causes the arm 61 to flex radially inward and urge pawl 60 into engagement with the teeth on the plunger 5. When the housing 120 is removed to fit a new cartridge 100, this allows the sleeve 64 to move forward under the thrust of the spring so that collet 63 moves forward of release stop 67 and bears against the inclined face 62 to lift the pawl 60 clear of the teeth on the plunger 5. The plunger 5 can now be retracted into the device to enable another cartridge 100 to be fitted. By using the rear of the accurately molded housing 120 to actuate the pawl mechanism 60–67, rather than the rim of the cartridge 100, variations in the size of the cartridge 100 can be accommodated.

Rearwardly of shoulder 20, the body of the device houses the plunger drive mechanism, the means for engaging and disengaging the drive mechanism from the plunger, and the dosage selection means. In the form of the device shown, these take the form of a series of members concentrically journalled around the plunger 5.

As shown the housing comprises a rotatable section 6 which houses the drive engagement mechanism; a fixed section 7 containing the dosage selection mechanism and having a port 8 through which a scale 9 indicating the dose selected can be seen by the user; a further rotatable collar or sleeve 10 for operating the dosage selection mechanism: and a terminal axially operating push button 11 for driving the plunger 5 forward to dispense the selected dose. The various sections of the housing can have any desired external shape, but it is preferred that the housing 1, sleeve 6 and section 7 have an oval external cross-section so that the relative rotational position of one with respect to the other can readily be detected by a user, notably by a blind person.

The plunger 5 preferably has a substantially circular cross-section but can have a squared, triangular or other cross-section shape if desired. For example, as shown in FIG. 15, it may have two opposed flats along its length to guide the drive means.

The plunger 5 carries a series of circumferential ribs or teeth 22 which form an axial ratchet into which the one-way mechanism 21 and the radially clampable drive mechanism described below engage. The teeth 22 are of a saw tooth form with a scarp face of the teeth directed rearwardly. Preferably, the teeth extend axially for the full length of the plunger 5. It is preferred that the axial distance from one tooth to the next corresponds to a dosage unit for the material being dispensed.

Located to the rear of shoulder 20 is the drive mechanism and the mechanism for engaging and disengaging this from the plunger. The drive mechanism is a pawl type mechanism which is radially engageable and disengageable with the teeth on the plunger and comprises two jaws 23 and 24 diametrically opposed to one another and carrying on their radially inward faces teeth which correspond to and engage with the teeth 22 on the plunger.

The jaws are normally urged radially outwardly, as shown for jaw 24 in FIG. 14, by transverse coil springs acting between the jaws 23 and 24 or by other bias means (not shown) so that their teeth do not engage those of the plunger which is then free to move axially with respect to the jaws when they are in their outward position, but is locked to the jaws when they are in their radially inward position, as shown for jaw 23 in FIG. 14.

The jaws are moved radially inward against the thrust of the coil springs by a pair of cams carried on the internal face of the rotatable section 6 of the housing or formed by the narrower diameter sectors of the oval cross-section of the rotatable section 6. The user has to twist section 6 to engage or disengage the jaws from plunger 5 and thus engage or disengage the drive to the plunger. If desired, section 6 can be spring biassed towards the drive disengaging position so that the user always has to twist section 6 before the device can be used.

The shoulder 20, as shown in FIG. 14, defines the forward limit of the travel of the drive mechanism and provides the datum point from which the dosage is determined. In the device shown in FIGS. 14 and 15 the forward faces of jaws 23 and 24 butt against the rear face of shoulder 20 to set the zero or datum point for the dosage selection mechanism.

A push sleeve 25 journalled on plunger 5 and within the dosage selection mechanism described below acts axially on the rear faces of the jaws 23 and 24 when in their drive engaged position to drive the jaws and hence the plunger 5 forward. When the jaws are in the drive disengaged position, they still bear against the push sleeve so that they carry it axially rearwards with them during the dosage selection. The push sleeve 25 provides the mechanical link between the terminal push button 11 which a user presses and the jaws 23 and 24.

The jaws 23 and 24 are moved axially by means of a split jaw drive sleeve 26 which has forward hooks 27 which engage similar recesses 28 at the rear of the jaws and rearward hooks 29 or other flexible linkages which connect the sleeve 26 axially to the forward end of the screw sleeve 30 of the dosage selection mechanism. When the jaws are in the drive disengaged position as shown for jaw 24 in FIG. 14 the hooks 27 and recesses 28 are engaged and the jaws can be moved axially with the screw sleeve 30. When the jaws are in the drive engaged position, as shown for jaw 23 in FIG. 14, the hooks 27 are released from recesses 28 to permit the jaws to move axially with sleeve 25 and free from the screw sleeve 30.

The dosage selection mechanism is housed within section 7 of the housing and comprises a screw sleeve 30 journalled for rotation and axial movement upon push sleeve 25. Sleeve 30 carries an external screw thread 31 which engages a similar thread 32 carried internally by section 7 of the body of the device. Sleeve 30 is rotated and thus caused to move axially by means of a collar driving the sleeve through a spined drive 33 shown in FIG. 15. The window insert in port 8 preferably has a ratchet or clicker mechanism 34 to give an audible indication as the dose is selected.

Retraction of sleeve 30 carries the jaw drive sleeve 26 and the jaws 23 and 24 with it when they are in the

disengaged position and the dose selected can be seen through port 8. Re-engagement of jaws 23 and 24 with the plunger breaks the latch 27/28 and allows the push sleeve 25 and the jaws 23 and 24 to move independently of the screw sleeve 30 and the jaw drive sleeve 26.

To indicate when there is insufficient fluid left in the cartridge to achieve the next dose, a radial shoulder or stop 50 is located at or adjacent the rearward end of plunger 5. This co-operates with a corresponding stop or shoulder 51 at the forward end of the push sleeve 25. The stops engage when the push sleeve is retracted to the maximum extent possible as the plunger 5 approaches the extreme of its forward travel. The user can then see from the dose displayed at the port 8 whether the cartridge contains the requisite amount of fluid. Since the plunger drive is not engaged at this time, the user can then set the dosage mechanism to the required dose if this is less than the amount indicated as remaining in the cartridge without having to discharge fluid as with a conventional device.

Push sleeve 25 is provided with a push button end cap 11 protruding axially from the body of the device which the user depresses to drive the sleeve 25 forward within the housing until the front face of jaws 23 and 24 butt against the rear of shoulder 20. The jaws 23 and 24 can only be moved rearwardly when they have been disengaged from the teeth 22 on the plunger 5, since the one-way mechanism will prevent rearward movement of the plunger 5. If a user attempts to set the dosage mechanism while the drive is engaged, he will detect resistance to rotation of sleeve 10. If he ignores this, the spline drive 33 between collar 10 and the screw sleeve 30 will be over-ridden to release the screw sleeve to prevent damage to the mechanism. However, unless the drive is engaged, depression of button 11 will not achieve any forward movement of the jaws or discharge of fluid from the cartridge 100.

The above device can be manufactured in many suitable materials and readily lends itself to manufacture by injection molding of suitable plastics materials with the various components being snap fits upon one another.

In operation, a user initially prepares the dispensing device for use by removing the holder 120, inserting a cartridge 100 in the holder 120, and then screwing the holder 120 into place on the collar 2b. The needle assembly 150 is then screwed into place on the housing 120. The user then rotates the sleeve 6 to disengage the drive mechanism if this has not already been done. Jaws 23 and 24 should be seated against the rear face of shoulder 20, the zero setting, from the previous use of the device, but the screw sleeve 30 will be at the dosage position previously selected. The user can thus see what dose was last administered where a sequence of different doses has to be administered. Collar 10 is rotated, say clockwise, to bring sleeve 30 to its forward position at which the latching mechanism 27/28 engages the jaws 23 and 24 and seats them firmly against the rear face of stop 20. The engagement of the latches can be used to provide an audible signal when this occurs, or the resistance to further forward movement will provide the signal to the user that the zero setting has been reached. The dosage displayed through port 8 will now read zero.

Collar 10 is then rotated counter-clockwise the desired number of turns, as evidenced by the number of clicks heard or by the dose displayed at the port 8, to retract screw sleeve 30, the jaw drive sleeve 26 and the jaws 23 and 24 and the push sleeve 25 the desired distance with respect to plunger 5. This will also cause the push button 11 to be extended from the rear end of the device. If the user inadvertently turns the collar 10 too far, it can be rotated clockwise to the correct position without moving the plunger.

Sleeve 6 is then rotated to re-engage the positive drive between the push sleeve 25, the jaws 23 and 24 and the plunger 5. This action will also disengage the latch 27/28 between jaws 23 and 24 and the jaw drive sleeve 26. At this point the device is cocked and ready to dispense the desired dose from the cartridge. However, the device has required a series of positive actions to achieve this state and would not normally be retained by a user in the cocked state, but would be stored with the drive disengaged so that accidental actuation of the device can not occur.

The user then inserts the point of needle 3 into his arm, buttock or other suitable point in his body and depresses button 11 to administer the dose of insulin. The dose is administered by depressing the button fully. If the button is not depressed fully, the user can detect this and can complete the dose administration. If desired, a colored band can be mounted around button 11 which will remain partially exposed until the button is fully depressed. Release of pressure on button 11 does not allow the plunger 5 to retract as with previous designs, so that jerky or interrupted depression of button 11 does not allow the user to pump the device to administer an excessive dose.

When the full dose has been administered, the jaws 23 and 24 will butt against the rear of shoulder 20. Due to the action of the one-way mechanism 21. 60–67, the blocks 23 and 24 cannot be retracted and administration of a further dose of insulin is not possible until the whole process of dose selection and re-cocking of the device is carried out. The device will therefore resist accidental overdosing due to repeated pressing of button 11.

As stated above, the cartridge-holder assembly of this invention finds use wherever it is desired to provide a removable cartridge for a measured dose syringe, for example in the administration of other medicaments or in dispensing accurately known amounts of a fluid, for example in blood tests or analytical work. It will also be appreciated that the assembly may be altered in ways which do not affect the fundamental operating concept of the assembly, for example by using other materials and configurations.

It is therefore intended that the foregoing detailed description be regarded as illustrative rather than limiting, and that it be understood that it is the following claims, including all equivalents, which are intended to define the scope of this invention.

I claim:

1. A cartridge assembly for a syringe-type medication dispensing unit, said assembly comprising:

a cartridge comprising a cartridge body having first and second ends, a pierceable membrane mounted at the first end, and a piston mounted at the second end, with a volume of mediation contained in the cartridge body between the membrane and the piston;

a cartridge holder having first and second ends, said first holder end defining a central opening and means for mounting a double ended needle, said second holder end defining means for securing the holder to a medication dispensing unit and an actuating shoulder, said holder defining a central cavity;

one of said central cavity and said cartridge being shaped with a plurality of raised lands adapted to frictionally to engage the opposed surface of the other of said cartridge and cavity so as to form an assembly which can be handled as a single modular unit with the cartridge held securely in the holder.

2. The invention of claim 1 wherein the double ended needle mounting means comprises a first set of external threads.

3. The invention of claim 1 wherein the holder securing means comprises a second set of external threads.

4. A cartridge assembly for a syringe-type medication dispensing unit, said assembly comprising:

a cartridge comprising a cartridge body having first and second ends, a pierceable membrane mounted at the first end, and a piston mounted at the second end, with a volume of medication contained in the cartridge body between the membrane and the piston;

a cartridge holder having first and second ends, said first holder end defining a central opening and means for mounting a double ended needle, said second holder end defining means for securing the holder to a medication dispensing unit and an actuating shoulder, said holder defining a central cavity shaped to receive and frictionally engage the cartridge to form an assembly which can be handled as a single, modular unit with the cartridge held securely in the holder;

wherein the holder securing means comprises a second set of external threads; and

wherein the modular unit is mounted to a syringe type medication dispensing unit having a plunger engageable with the piston, a one-way mechanism engaged with the plunger, and an actuating member for the one-way mechanism, wherein the second holder end is received within the dispensing unit, wherein the second set of external threads is engaged with the dispensing unit, and wherein the actuating shoulder is engaged with the actuating member.

5. The invention of claim 4 wherein the dispensing unit and the holder define a detent system which holds the second set of external threads in engagement with the dispensing unit.

6. The invention of claim 5 wherein the detent system comprises inter engaging ramps on the holder and the dispensing device adjacent the second set of external threads.

7. The invention of claim 1 wherein the modular unit is mounted to a cap which encloses the first end of the holder, wherein the holder defines at least one stop member wherein the cap defines at least one lug, wherein at least one of the stop member and lug has a transverse face and a sloping face oriented such that the stop member and lug abut at the transverse face to limit rotation of the cap when the cap is rotated in a first direction with respect to the holder, and the stop member and the lug abut at the sloping face to shift the cap axially along the holder when the cap is rotated in a second direction with respect to the holder.

8. The invention of claim 1 wherein the modular unit is mounted to a cap which encloses the first end of the holder; wherein one of the holder and the cap defines at least one groove having an axial portion and a circumferential portion; and wherein the other of the holder and the cap defines a protruding element shaped to slide in the groove to secure the cap and holder together in a bayonet mount.

9. The invention of claim 1 wherein the holder frictionally engages only the first end of the cartridge.

10. The invention of claim 9 wherein the cartridge defines an annular collar disposed around the membrane, and wherein the holder frictionally engages the cartridge only at the collar.

11. The invention of claim 10 wherein the plurality of raised lands are positioned on the holder to frictionally engage the collar.

12. The invention of claim 2 further comprising:

a needle assembly comprising a double ended needle secured to a mounting element which defines a set of internal threads engaged with the first set of external threads of the holder, with one end of the needle passing through the membrane and in contact with the medication.

13. The invention of claim 1 wherein the medication comprises an insulin solution.

14. The invention of claim 1 wherein the second end of the cartridge extends out of the holder by a distance of about ½ inch or more.

15. A cartridge assembly for a syringe-type medication dispensing unit, said assembly comprising:

a cartridge comprising a cartridge body having first and second ends, a pierceable membrane mounted at the first end, and a piston mounted at the second end, with a volume of medication contained in the cartridge body between the membrane and the piston and an annular collar disposed around the membrane;

a cartridge holder having first and second ends, said first holder end defining a central opening and a first set of external threads, said second holder end defining an actuating shoulder and a second set of external threads said holder defining a central cavity shaped to receive the cartridge with the pierceable membrane adjacent the central opening, said cartridge having a length greater than that of the holder such that the second end of the cartridge extends out of the holder,

said holder defining a plurality of raised lands positioned to frictionally engage the collar to form an assembly which can be handled as a single, modular unit with the cartridge held removably in the holder by friction between the collar and the holder, said holder shaped to receive the cartridge freely until the lands engage the collar, such that the weight of the cartridge will move the cartridge into the holder until the lands contact the collar.

16. The invention of claim 15 wherein the modular unit is mounted to a syringe type medication dispensing unit having a plunger engageable with the piston, a one-way mechanism engaged with the plunger, and a one-way mechanism actuating member, wherein the second hold end is received within the dispensing unit, wherein the second set of external threads is engaged with the dispensing unit, and wherein the actuating shoulder is engaged with the one-way mechanism actuating member.

17. The invention of claim 16 wherein the dispensing unit and the holder define a detent system which the second set of external threads in engagement with the dispensing unit.

18. The invention of claim 17 wherein the detent system comprises inter-engaging ramps on the holder

and the dispensing device adjacent the second set of external threads.

19. The invention of claim 18 wherein the modular unit is mounted to a cap which encloses the first end of the holder, wherein the holder defines at least one stop member, wherein the cap defines at least one lug, wherein at least one of the stop member and lug has a transverse face and a sloping face oriented such that the stop member and lug abut at the transverse face to limit rotation of the cap when the cap is rotated in a first direction with respect to the holder, and the stop member and the lug abut at the sloping face to shift the cap axially along the holder when the cap is rotated in a second direction with respect to the holder.

20. The invention of claim 15 wherein the modular unit is mounted to a cap which encloses the first end of the holder; wherein one of the holder and the cap defines at least one groove having an axial portion and a circumferential portion; and wherein the other of the holder and the cap defines a protruding element shaped to slide in the groove to secure the cap and holder together in a bayonet mount.

21. The invention of claim 15 further comprising:

a needle assembly comprising a double ended needle secured to amounting element which defines a set of internal threads engaged with the first set of external threades of the holder, with one end of the needle passing through the membrane and in contact with the medication.

22. The invention of claim 15 wherein the medication comprises insulin.

23. The invention of claim 15 wherein the lands are axially oriented.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 4,936,833

DATED : June 26, 1990

INVENTOR(S) : Bernard Sams

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

IN THE CLAIMS

Col. 10, line 59, claim 1, delete "mediation" and substitute therefor --medication--;

Col. 12, line 58, claim 16, delete "hold" and substitute therefor --holder--.

Col. 12, line 64, claim 17, after "which" insert --holds--.

Col. 14, line 8, claim 21, delete "amounting" and substitute therefor --a mounting--.

Col. 14, line 10, claim 21, delete "threades" and substitute therefor --threads--.

Signed and Sealed this

Twenty-second Day of December, 1992

Attest:

Attesting Officer

DOUGLAS B. COMER

Acting Commissioner of Patents and Trademarks

EXHIBIT 15

US005549575A

United States Patent [19]

Giambattista et al.

[11] Patent Number: 5,549,575

[45] Date of Patent: Aug. 27, 1996

[54] **CARTRIDGE RETAINER ASSEMBLY FOR MEDICATION DELIVERY PEN**

[75] Inventors: **Lucio Giambattista**, East Hanover; **Theodore Siuta**, Brant Beach, both of N.J.

[73] Assignee: **Becton Dickinson and Company**, Franklin Lakes, N.J.

[21] Appl. No.: **304,953**

[22] Filed: **Sep. 13, 1994**

[51] **Int. Cl.**[6] **A61M 5/00**

[52] **U.S. Cl.** **604/232**; 604/206; 604/241

[58] **Field of Search** 604/232, 234, 604/206–211, 240–243, 181, 187, 199–201, 71, 72, 131–136, 139, 218, 905

[56] **References Cited**

U.S. PATENT DOCUMENTS

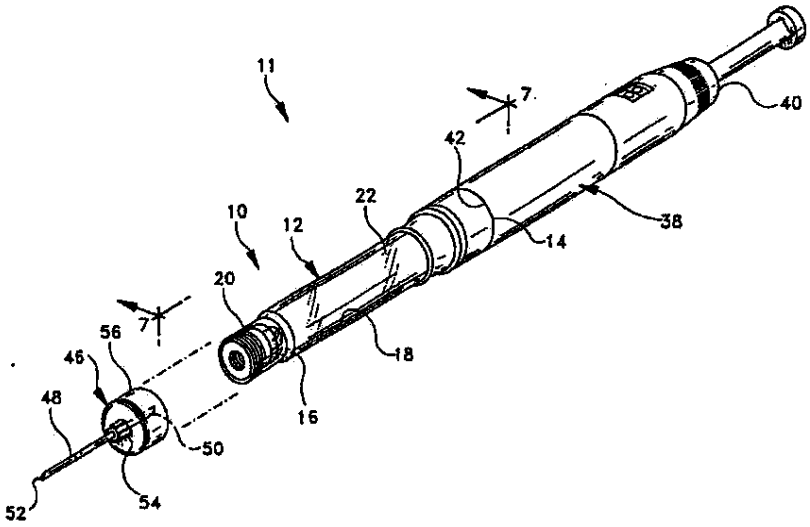
4,973,318	11/1990	Holm et al.	604/208
5,041,088	8/1991	Ritson et al.	604/135
5,085,641	2/1992	Sarnoff et al.	604/135
5,281,198	1/1994	Haber et al.	604/232
5,360,410	11/1994	Wacks	604/205

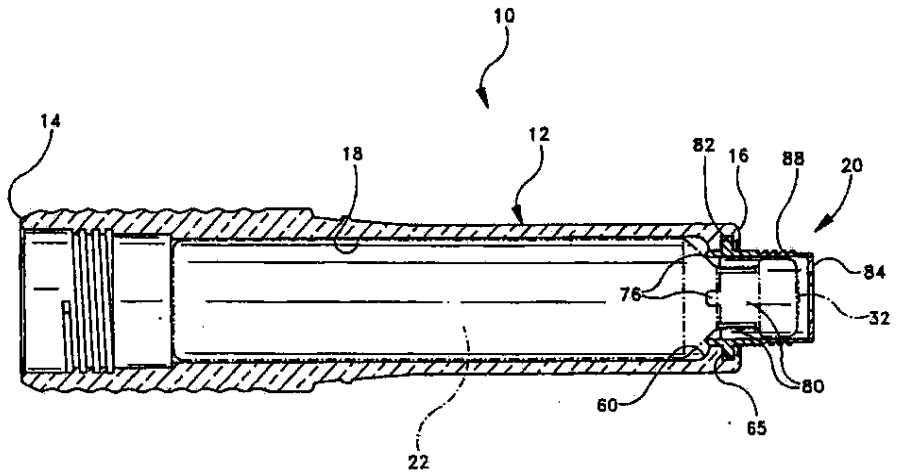
Primary Examiner—John D. Yasko
Assistant Examiner—Ronald K. Stright, Jr.
Attorney, Agent, or Firm—Alan W. Fiedler

[57] **ABSTRACT**

A cartridge retainer assembly is provided for a medication delivery pen. The cartridge retainer assembly includes a generally tubular body for receiving, supporting and accurately positioning the body and shoulder portions of a cartridge of medication. A needle mounting collar is floatably mounted to the body of the cartridge retainer assembly for receiving the neck, rubber septum and crimped metallic sleeve of the cartridge. The needle mounting collar will float into a position which compensates for eccentricities and dimensional variations of the cartridge.

9 Claims, 5 Drawing Sheets





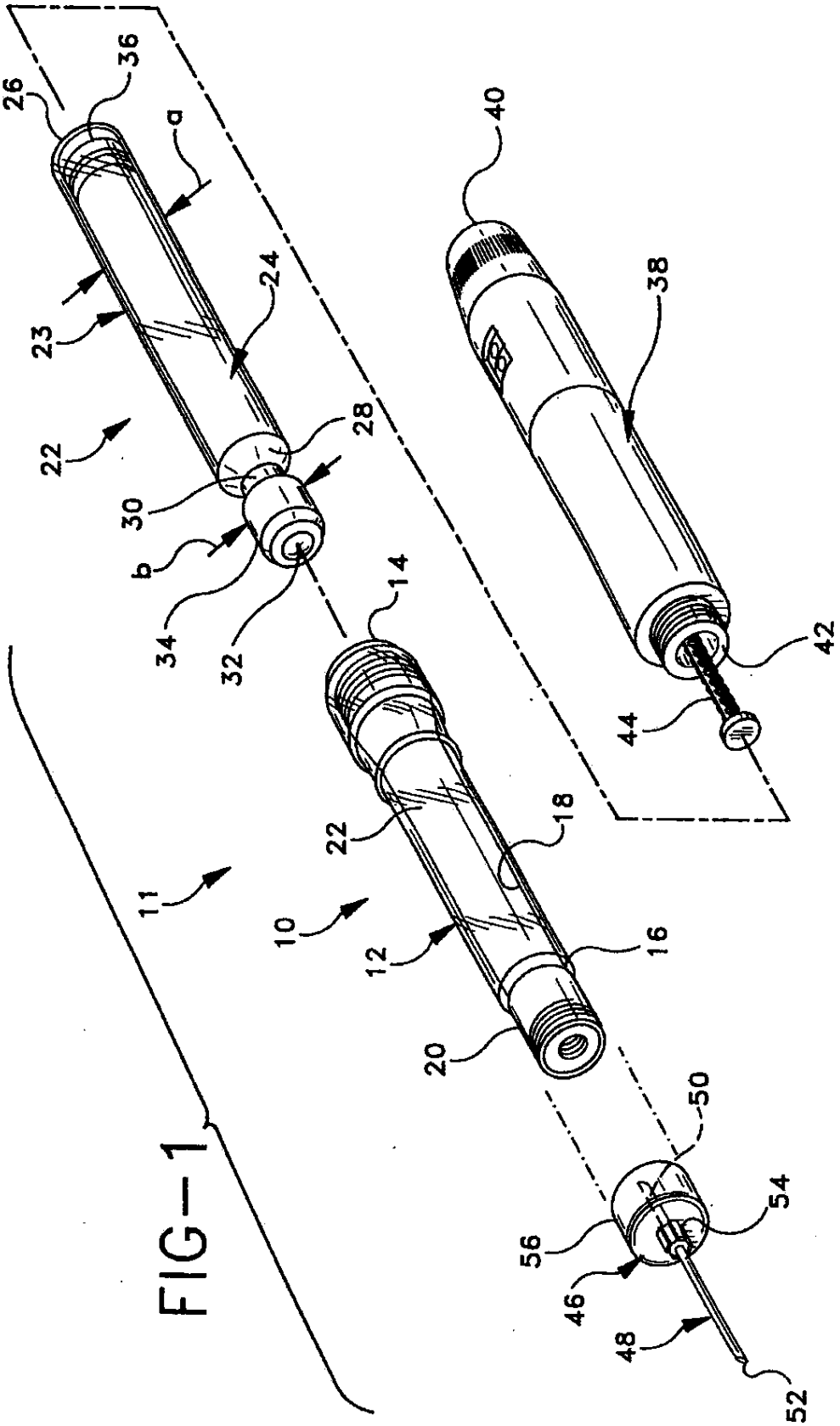

26
36
a
24
23
22
28
30
b
34
32
14
40
38
42
44
22
18
11
10
12
16
20
50
54
56
46
48
52

FIG-1

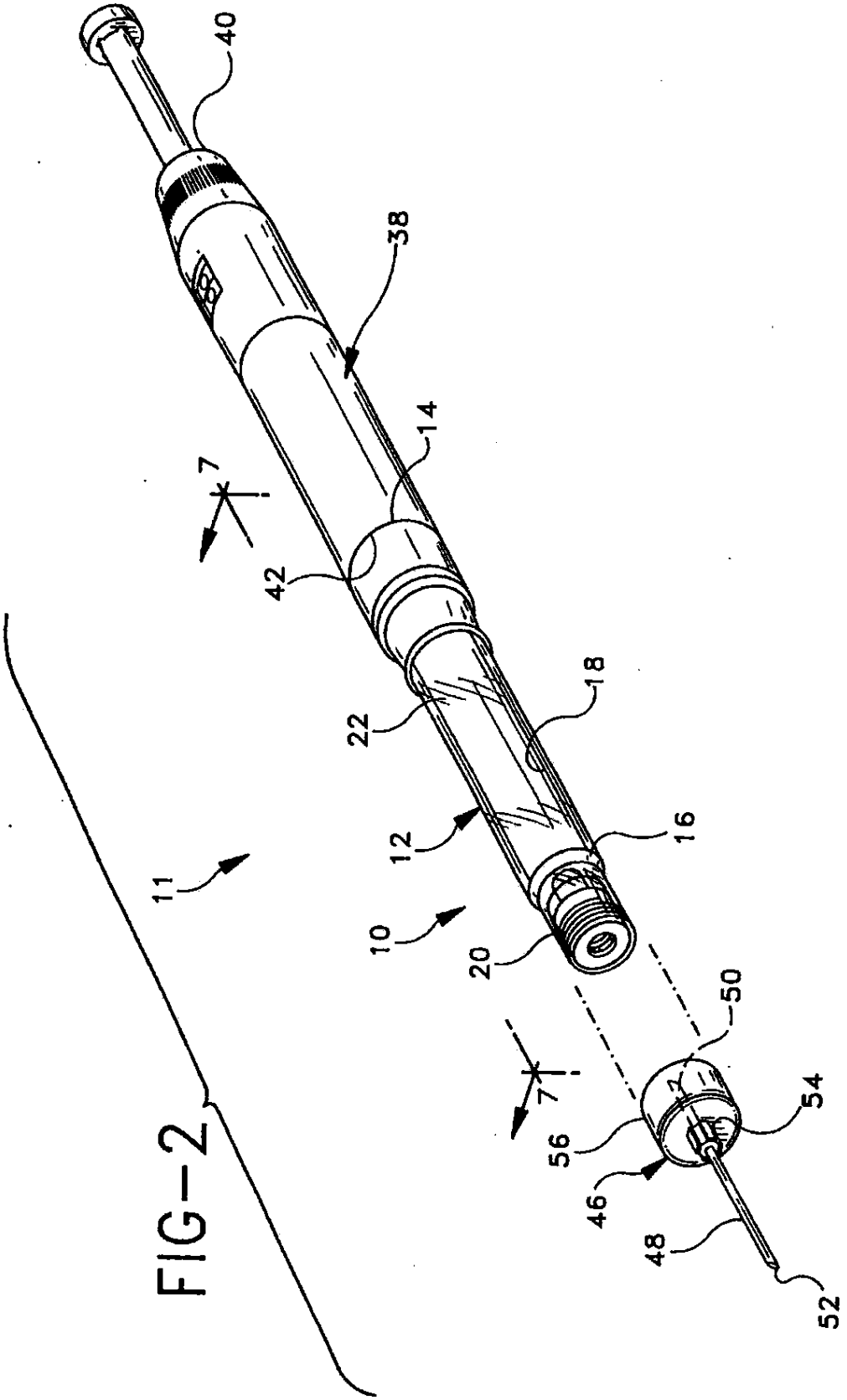


FIG-2

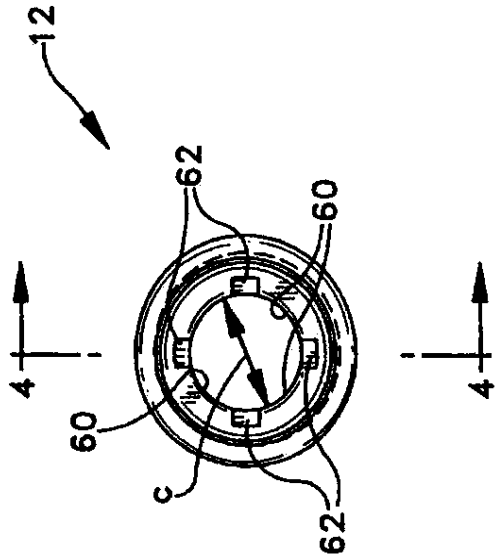


FIG-3

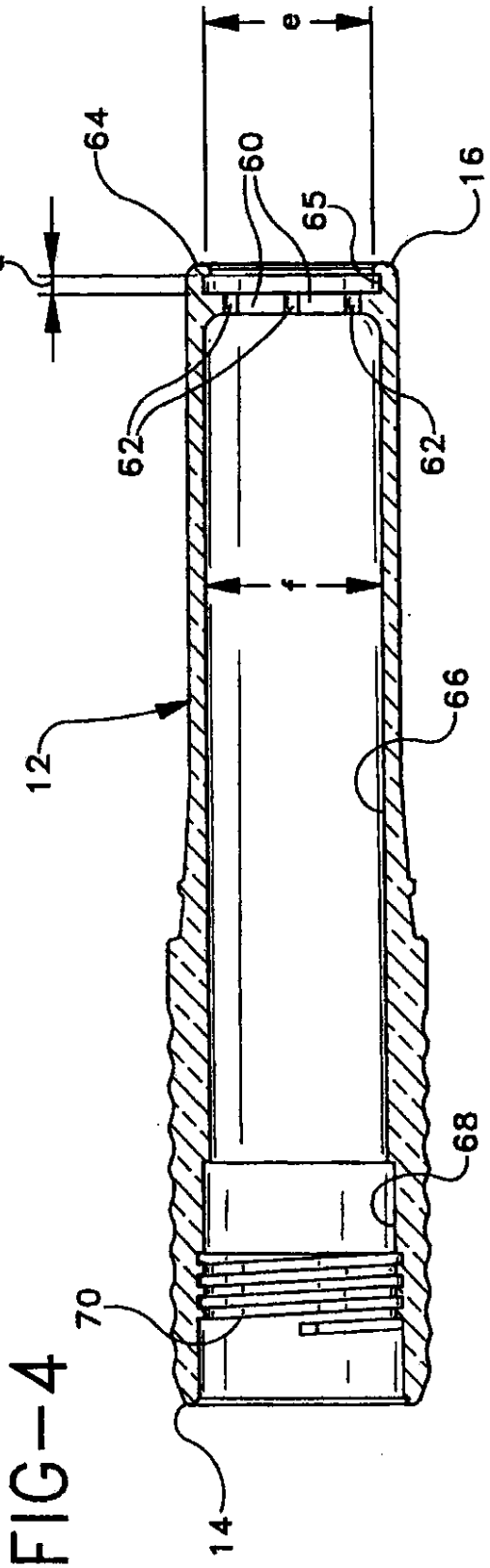


FIG-4

FIG-6

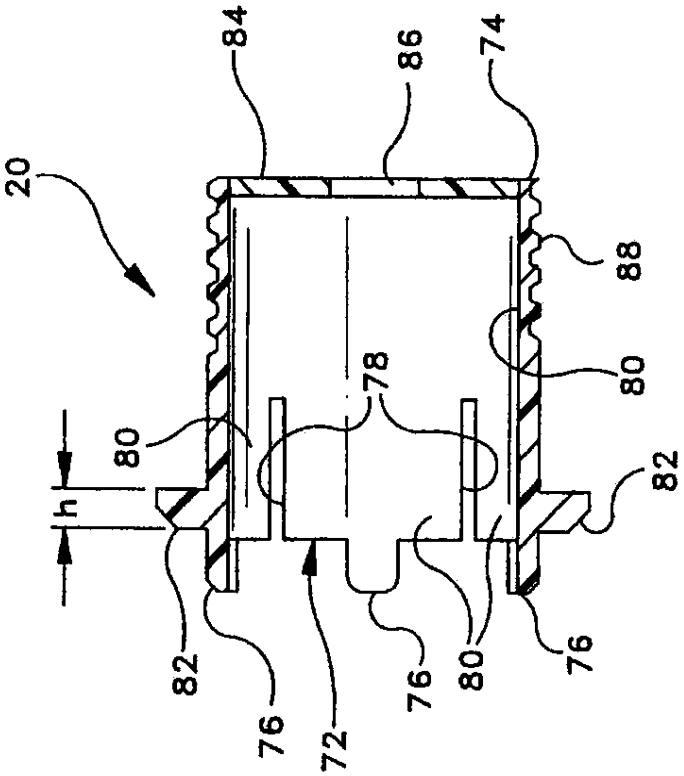
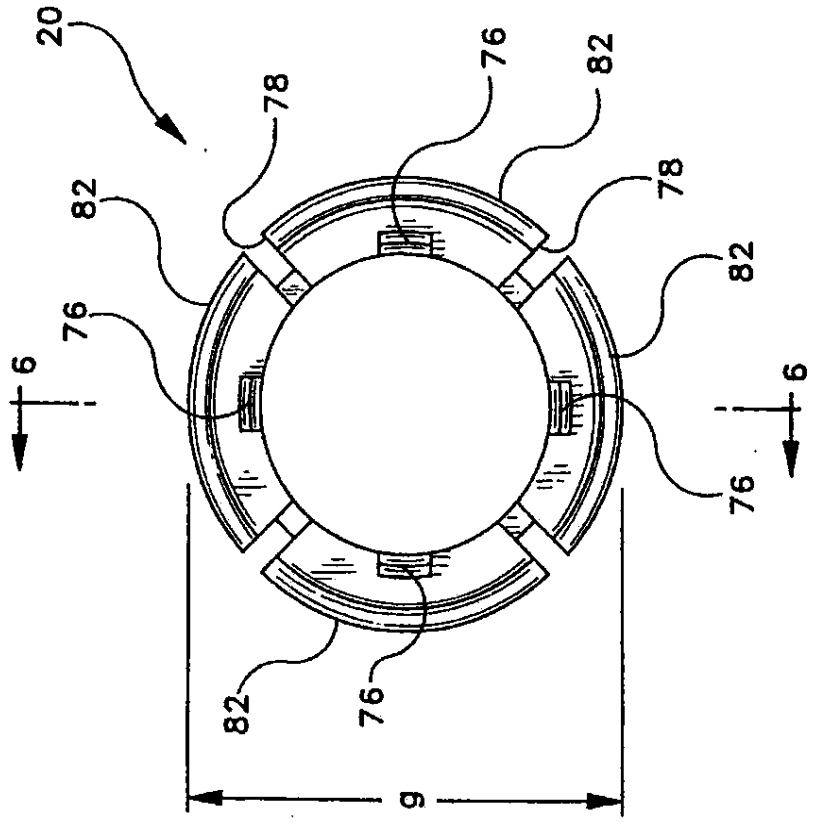
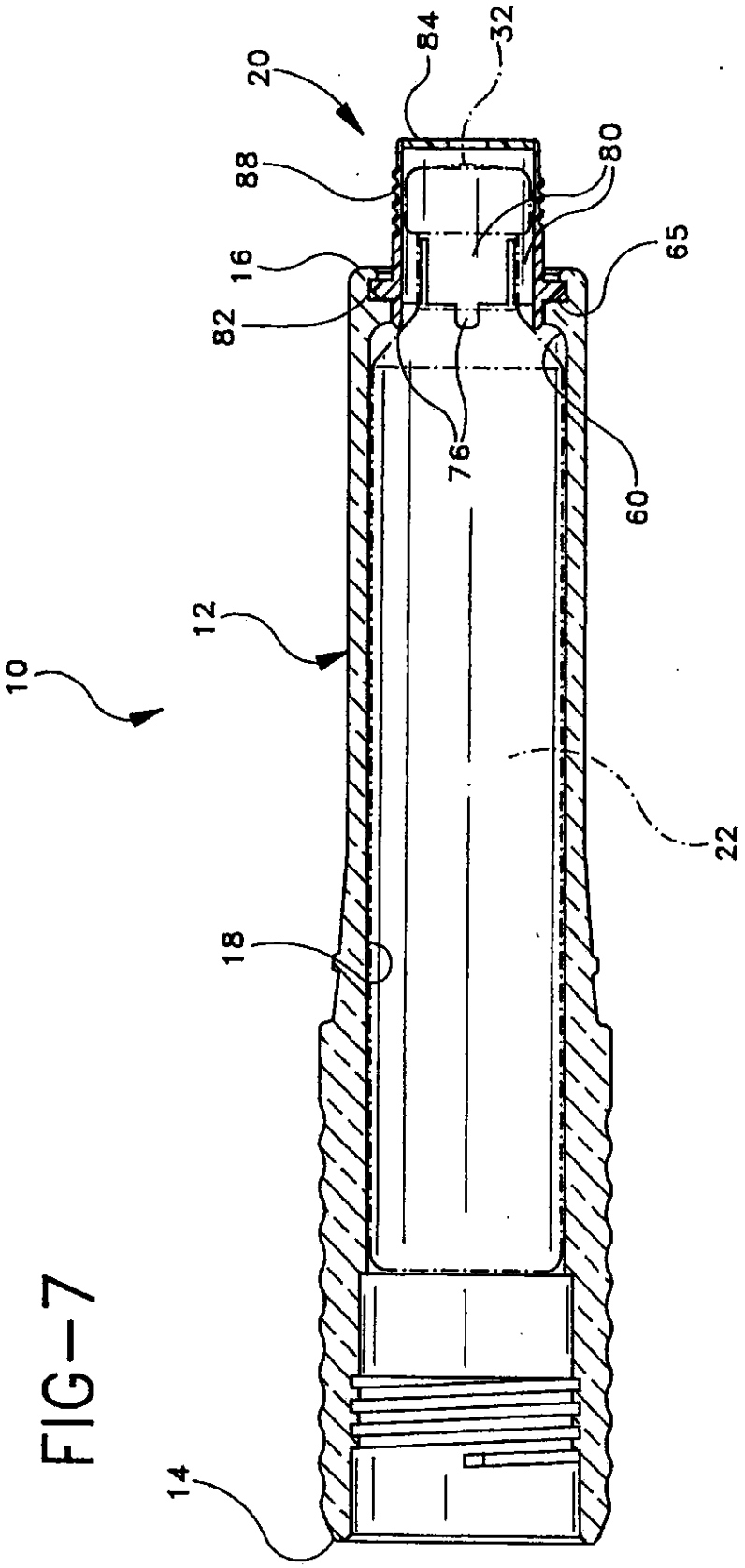

84
86
74
20
88
80
78
80
h
82
82
76
72
76
80
76

FIG-5


20
78
76
82
82
78
82
76
6
6
76
82
76
9



FIG—7

CARTRIDGE RETAINER ASSEMBLY FOR MEDICATION DELIVERY PEN

BACKGROUND OF THE INVENTION

1. Field of the Invention

The subject invention relates to the portion of a medication delivery pen that retains the cartridge of medication.

2. Description of the Prior Art

Medication delivery pens are hypodermic syringes that are used for self-injection of precisely measured doses of medication. Pens are widely used, for example, by diabetics to dispense insulin.

The typical prior art medication delivery pen includes a cartridge which contains a volume of liquid medication sufficient for several doses. The prior art cartridge includes an elongated generally tubular glass vial having an open proximal end and an opposed open distal end. The vial includes a large diameter barrel extending distally from the open proximal end to an inwardly tapering shoulder between the two ends. A short small diameter neck extends from the shoulder to the open distal end. The neck of the prior art vial has an annular rim projecting outwardly around the extreme distal end.

The prior art cartridge further includes a pierceable rubber septum which extends across the open distal end of the prior art vial, and is securely held in position by a metallic sleeve that is crimped to the annular rim on the tubular neck. The vial of the prior art cartridge is filled with liquid medication, and a rubber stopper is inserted into the open proximal end of the vial for sliding fluid-tight engagement with interior walls of the barrel.

The prior art medication delivery pen includes a unitarily molded cartridge retainer with opposed proximal and distal ends. A large diameter tubular body extends distally from the proximal end and is dimensioned for receiving the barrel of the vial. A short smaller diameter tubular neck is disposed distally of the body and is dimensioned for tightly engaging the tubular neck of the vial and the metallic sleeve crimped thereon so as to support and position the entire cartridge. Exterior regions at the extreme distal end of the tubular neck are formed with an array of threads for threadedly receiving the mounting cap of a needle assembly.

The prior art medication delivery pen further includes a dosing apparatus that is engaged with the proximal end of the cartridge retainer. The prior art dosing apparatus includes a plunger for engaging the rubber stopper of the cartridge, dose setting structure for selecting the longitudinal distance through which the plunger will move, and dispensing means for driving the plunger the selected distance. The prior art dosing apparatus may be permanently connected to prior art cartridge retainer with the cartridge therein. This type of prior art pen is used until the medication is exhausted and then the entire pen is discarded. Other prior art medication delivery pens may have the dosing apparatus removably connected to the cartridge retainer so that at least portions of the pen may be reused when the medication in the cartridge is exhausted.

Prior art needle assemblies for medication delivery pens are safely sealed in packages. A needle assembly is accessed immediately prior to an injection, and is discarded immediately after the injection. The prior art needle assembly for medication delivery pens includes an elongate needle cannula having opposed proximal and distal points and a lumen extending therethrough. A plastic cork is adhered to an intermediate position along the needle cannula and in turn is rigidly connected to an end wall of a cylindrical cap. The cylindrical wall of the cap surrounds the proximal point on the needle cannula and includes an array of internal threads for engaging the external threads on the neck of the prior art cartridge retainer.

The prior art medication delivery pen may be used by opening the sealed needle assembly and urging the cap over the neck of the vial retainer sufficiently for the proximal point of the needle cannula to pierce the rubber septum of the prior art cartridge. The cap is then rotated to threadedly engage the neck of the prior art cartridge retainer. The user will then manipulate the dosing apparatus to select an appropriate dose. A protective shield over the distal end of the needle cannula is then removed, and the distal point of the needle cannula is injected. The user then actuates the dispensing means of the prior art dosing apparatus to urge the stopper of the cartridge distally and to deliver medication through the lumen of the needle cannula. The needle is then withdrawn, and the needle assembly is separated from the cartridge retainer and safely discarded. The rubber septum of the cartridge will reseal itself, and may be pierced again for a subsequent administration of medication. This process may be carried out repeatedly until all of the medication in the cartridge has been used.

The neck at the distal end of the prior art unitarily molded cartridge retainer has been precisely formed to closely engage, support and position the entire cartridge. However, cartridges are subject to a considerable range of dimensional variations and a considerable degree of eccentricity. These dimensional variations and eccentricities may be due to the glass vial manufacturing processes or to the crimping of the metallic sleeve that holds the rubber septum in place. Dimensional variations can result in a cartridge that will not fit the cartridge retainer or that will be loosely supported and movable therein. Eccentricities can result in a vial barrel that is not properly positioned or aligned within the body of the cartridge retainer. Eccentricities also can prevent the neck of the vial from sliding into the precisely dimensioned neck of the cartridge retainer. As a result, considerable quality control efforts must be undertaken to ensure that only cartridges that are within narrowly defined dimensional tolerances are used, and high reject rates occur. To reduce rejects and ensure that a larger number of vials can be accepted, prior art pens have included vial retainers with wider bodies that are intended to accommodate a greater range of eccentricities between the neck and the body of the vial. This results in larger pens even though it would be desirable to reduce the size.

Users of medication delivery pens are urged to disinfect both the puncture site and the distal end of the pen prior to each injection of medication. The disinfectant can react with the plastic of the prior art cartridge retainer to cause crazing or cracking.

Medication delivery pens also have been found to exhibit weeping or drooling near the interface of the needle assembly and the cartridge retainer. This weeping or drooling presents inconveniences to the user and creates the potential for an accumulation of medication at an external position on the pen and near the puncture site of the patient.

It is now believed that weeping or drooling is attributable to contact between the septum and the cork of the needle assembly during the injection of medication. In particular, the movement of the plunger distally in the vial urges the liquid in a distal direction. These distally directed forces urge liquid through the lumen of the needle cannula. How-

ever, these forces also cause a stretching of the septum in a distal direction. As noted above, the neck of the prior art cartridge retainer provides the primary support for the cartridge, and hence closely engages the metal sleeve which holds the septum to the vial. The distal stretching of the septum in response to fluid pressure urges the septum into direct contact with the cork on the needle assembly of the prior art medication delivery pen. The combination of fluid pressure and contact with the cork will sufficiently change the shape of the pierced septum to permit the weeping or drooling of medication between the septum and the needle cannula.

Still another problem with prior art medication delivery pens relates to the above described disposition of threads around the distal end of the prior art cartridge retainer. In particular, the threads begin at the distal tip of the prior art cartridge retainer and extend a short distance in a proximal direction. Even minor variations in dimensional tolerances can require the user to threadedly engage the cap of the needle assembly to the threads of the cartridge retainer before the proximal tip of the needle cannula has pierced the septum. In these instances, the beveled proximal tip of the needle cannula will pierce the septum while undergoing a rotational movement. This may cause the beveled tip to rip the septum and may further contribute to the above described drooling or weeping. Sufficiently large rips may not adequately reseal and can lead to a premature degradation of the medication stored in the vial.

SUMMARY OF THE INVENTION

The subject invention is directed to a two-piece cartridge retainer assembly that is particularly suitable for medication delivery pens. The cartridge retainer assembly includes a generally tubular body for surrounding the barrel of a vial and for supportingly engaging the converging wall that defines the shoulder of the vial. The cartridge retainer assembly further includes a needle mounting collar floatingly mounted to the body for surrounding the neck of the vial. The needle mounting collar may be diametrically dimensioned to closely engage the metallic sleeve which is crimped to the vial for holding the rubber septum in place. However, such close engagement is not essential. The needle mounting collar of the cartridge retainer assembly may also define an axial length for preventing contact between the rubber septum and the cap or cork of the needle assembly. Thus, drooling or weeping in response to contact between a distended septum and the cork of the needle assembly is substantially eliminated.

Floating between the needle mounting collar and the body of the cartridge retainer assembly enables the cartridge retainer assembly to accommodate a much greater range of eccentricities. Hence, the diametrical dimensions of the body of the cartridge retainer assembly can be reduced. Additionally, the two-piece design for the cartridge retainer assembly enables dissimilar materials to be used for the body and the needle mounting collar. For example, the body may be formed from any convenient transparent plastic material that will provide the necessary structural support and that will enable observation of the stopper positioned within the vial. The needle mounting collar, on the other hand, may be formed either from a thin metal or a plastic that exhibits appropriate resistance to disinfectants that may be used before or after each injection.

The secure but floatable connection of the needle mounting collar to the body may be achieved by a plurality of axial extending slots formed either on the body or the needle mounting collar of the cartridge retainer. The slots may define resiliently deflectable fingers. Each finger may be provided with tabs disposed and dimensioned to be snap fit into corresponding grooves in the opposing member. The tabs and grooves will prevent unintended axial separation of the needle mounting collar and the body of the cartridge retainer assembly. However, the resiliently deflectable fingers will permit a certain range of radial movement to accommodate dimensional variations and eccentricities in the cartridge being retained. Preferably the external threads on the needle mounting collar of the cartridge retainer assembly are spaced proximally from the extreme distal end. This proximal position ensures that the proximal tip of the needle cannula can pierce the septum in response to axial movement of the needle assembly and without relative twisting that could cause ripping of the septum. The twisting for threaded engagement of the needle assembly and the needle mounting collar will be carried out only after the beveled tip is fully within the vial and beyond the position where rotation of the needle can urge the sharp beveled edges into ripping or tearing engagement with the rubber septum.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is an exploded perspective view of a medication delivery pen having a cartridge retainer assembly in accordance with the subject invention.

FIG. **2** is a perspective view of the assembled medication delivery pen incorporating the cartridge retainer assembly of the subject invention.

FIG. **3** is an end elevational view of the body of the cartridge retainer assembly.

FIG. **4** is a cross-sectional view taken along line **4—4** in FIG. **3**

FIG. **5** is an end elevational view of the needle mounting collar of the cartridge retainer assembly.

FIG. **6** is a cross-sectional view taken along line **6—6** in FIG. **5**.

FIG. **7** is a cross-sectional view taken along line **7—7** in FIG. **2**.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

A cartridge retainer assembly in accordance with the subject invention is identified generally by the numeral **10** in FIGS. **1–7**. Cartridge retainer assembly **10** is intended to be a part of a medication delivery pen **11** and includes elongate generally tubular body **12** with opposed proximal and distal ends **14** and **16** respectively and a cartridge receiving cavity **18** extending therebetween. A generally tubular needle mounting collar **20** is floatably mounted to distal end **16** of body **12**. Body **12** and collar **20** of cartridge retainer assembly **10** both are described in greater detail below.

Cartridge retainer assembly **10** is dimensioned and configured to receive a cartridge assembly **22** therein. Cartridge assembly **22** includes a vial **23** with a generally tubular barrel **24** of diameter "a" with an open proximal end **26** and a distal end defined by an inwardly converging shoulder **28**. A small diameter neck **30** projects distally from shoulder **28** of barrel **24** on vial **23**, and is provided with a large diameter annular bead (not shown) extending circumferentially thereabout at the extreme distal end of neck **30**. A pierceable and resealable rubber septum **32** extends completely across the open distal end defined by neck **30**. Rubber septum **32** is

held in place by a metallic sleeve **34** which is crimped around the circumferential bead at the distal end of neck **30**. Crimped metallic sleeve **34** defines an approximate diameter "b" which is less than diameter "a" of body **24**. Medication such as insulin or heparin is pre-filled into vial **23** and is retained therein by a rubber stopper **36**. Stopper **36** is in sliding fluid-tight engagement with the tubular wall of barrel **24**. Distally directed forces on stopper **36** urge the medication from pen **11** as explained further below.

Medication delivery pen **11** further includes a prior art dosing apparatus identified generally by the numeral **38**. Dosing apparatus **38** also is generally cylindrical and includes opposed proximal and distal ends **40** and **42** respectively. Threads are disposed at distal end **42** of prior art dosing apparatus **38** for releasable threaded engagement with proximal end **14** of body **12** of cartridge retainer assembly **10**, as shown in FIG. **2**. A plunger rod **44** projects distally from dosing apparatus **38** and is dimensioned to engage stopper **36** of cartridge assembly **22**. The prior art dosing apparatus **38** includes known mechanisms therein for setting a selected dose of medication to be delivered by pen **11**. A dispensing mechanism (not shown) is operative to drive plunger rod **44** a selected distance in a distal direction for moving stopper **36** a distance that will inject the selected dose of medication from cartridge assembly **22**. Although a particular prior art dosing apparatus **38** is depicted in FIGS. **1** and **2**, it is to be understood that other dosing apparatus can be used with the cartridge retainer assembly of the subject invention.

Medication delivery pen **11** further includes a prior art needle assembly **46** having a metallic needle cannula **48** with opposed proximal and distal tips **50** and **52** respectively and a lumen (not shown) extending entirely therethrough. A cork **54** is securely affixed at an intermediate position along needle cannula **48**, and a cap **56** is securely affixed to cork **54**. Cap **56** of prior art needle assembly **46** includes an array of internal threads (not shown) for removable mounting to cartridge retainer assembly **10**.

As explained above, prior art cartridge assemblies **22** are subject to significant dimensional variation and eccentricities. In particular, the crimped mounting of metal sleeve **34** to neck **30** can result in diametrical or axially length differences from one cartridge to the next. Additionally, considerable eccentricities between neck **30** and body **24** are likely to exist.

Cartridge retainer assembly **10** accommodates the dimensional variations and eccentricities that exist in prior art cartridge assemblies **22**. More particularly, as shown in FIGS. **3** and **4** body **12** of cartridge retainer assembly **10** includes a plurality of inwardly projecting supports **60** defining sections of arcs concentric with body **12**. Supports **60** define an inside diameter "c" which is greater than diameter "b" defined by crimped sleeve **34** of cartridge assembly **22**. Supports **60** are separated from one another by anti-rotation notches **62**. An inwardly projecting annular rim **64** is defined at the extreme distal end **16** of body **12** and in spaced relation to the supports **60**. Thus, an annular locking groove **65** with an axially measure thickness "d" and an inside diameter "e" is disposed intermediate supports **60** and rim **64**.

Portions of body **12** disposed proximally of supports **60** define a vial receiving chamber **66** of substantially uniform diameter "f" which is slightly greater than diameter "a" of vial barrel **24**. Portions of body **12** proximally of chamber **66** are of slightly larger diameter and define a recess **68** for receiving a portion of dosing apparatus **38**. An array of internal threads **70** in recess **68** engage threads on proximal end **42** of dosing apparatus **38**. It is to be understood, however, that other releasable engagement means between dosing apparatus **38** and cartridge retainer assembly **10** can be provided. For example, internal threads can be formed on dosing apparatus **38** and corresponding external threads can be defined on cartridge retainer assembly **10**.

Needle mounting collar **20** of vial retainer assembly **10** includes opposed proximal and distal ends **72** and **74** respectively as shown in FIGS. **5** and **6**. Proximal end **72** is characterized by a plurality of anti-rotation projections **76** dimensioned and disposed for sliding engagement in notches **62** between arcuate supports **60** near distal end **16** of cartridge retainer body **12**.

Needle mounting collar **20** further includes a plurality of spaced apart axially aligned slots **78** extending from proximal end **72** toward distal end **74**. Slots **78** define a plurality of proximally extending resiliently deflectable fingers **80** on proximal end **72** of collar **20**.

Proximal portions of deflectable fingers **80** are characterized by outwardly projecting locking ridges **82**. Each locking ridge **82** has an axially measured thickness "h" which is slightly less than the thickness "d" defined by locking groove **65** at distal end **16** of body **12**. Opposed locking ridges **82** further define an outside diameter "g" approximately equal to or slightly less than the diameter "e" defined by locking groove **65** in body **12**.

Distal end **74** of needle mounting collar **20** includes a generally annular end wall **84** having an aperture **86** extending therethrough for access by proximal point **50** of needle cannula **48**. An array of outwardly disposed threads **88** is defined intermediate proximal and distal ends **72** and **74** respectively. Threads **88** are disposed and dimensioned for engaging threads on prior art needle assembly **46**.

Needle mounting collar **20** and cartridge retainer body **12** are lockingly engaged with one another prior to sale of pen **11** by merely urging proximal end **72** of collar **20** into distal end **16** of body **12**. This assembly is carried out by first aligning anti-rotation projections **76** at proximal end **72** of collar **20** with anti-rotation notches **62** between supports **60** at distal end **16** of body **12**. After sufficient movement of collar **20** and body **12** toward one another, the chamfer on locking ridges **82** will engage annular rim **64** of body **12** to generate radially inward deflection of fingers **80**. After sufficient movement of collar **20** and body **12** toward one another, locking ridges **82** will pass proximally beyond rim **64**. Fingers **80** will then resiliently return toward an undeflected condition to lockingly engage ridges **82** in annular locking groove **65**.

Assembly of medication delivery pen **11** continues by inserting cartridge **22** into cartridge retainer assembly **10**. More particularly, neck **30** and crimped metallic sleeve **34** of vial **22** are inserted in a proximal to distal direction into open proximal end **14** of body **12** of the cartridge retainer assembly. Crimped metallic sleeve **34** eventually will pass entirely through body **12**, and further advancement of cartridge **22** into cartridge retainer assembly **10** will require entry of crimped metallic sleeve **34** into needle mounting collar **20**. As noted above, considerable dimensional variation and eccentricities between the neck and body of prior art vials are known to exist. If such eccentricities do exist, crimped metallic sleeve **34** will cause collar **20** to float radially relative to body **12** into a position that conforms with any dimensional inconsistencies or eccentricities in cartridge **22**. More particularly, forces generated by the distal advancement of cartridge **22** will cause resiliently deflectable fingers

80 of needle mounting collar 20 to deflect into a position that conforms with the actual location and alignment of crimped metallic sleeve 34. This floating movement will cause needle mounting collar 20 and body 12 of cartridge retainer assembly 10 to assume an eccentric alignment that conforms with an eccentrically aligned neck and body on a vial.

Further distally directed movement of vial 22 into cartridge retainer assembly 10 will cause shoulder 28 of cartridge 22 to seat against arcuate supports 60 of body 12. Supports 60 define the fully seated position of cartridge 22 in cartridge retainer assembly 10 and function to securely engage vial 22. In this fully seated position, as shown most clearly in FIG. 7, septum 32 of cartridge 22 is spaced proximally from distal wall 84 of needle mounting collar 20.

Dosing apparatus 38 may next be assembled to proximal end 14 of the body of cartridge retainer assembly 10 such that plunger rod 44 of dosing apparatus 38 engages stopper 36 of cartridge 22.

Medication delivery pen 11 may be used by mounting a needle assembly 46 to needle mounting collar 20 of cartridge retainer assembly 10. This mounting is achieved by moving needle assembly 46 in a proximal direction over needle mounting collar 20 until the threads (not shown) of cap 56 engage external threads 88 on needle mounting collar 20. As noted above, threads 88 of needle mounting collar 20 are spaced from the extreme distal end of needle mounting collar 20. Thus, the initial axial advancement of cap 56 over needle mounting collar 20 will cause proximal point 50 of needle cannula 48 to pierce rubber septum 32 of cartridge 22 prior to rotational threaded engagement of needle assembly 46 with needle mounting collar 20. Thus, the bevel which defines proximal point 50 will advance axially through septum 32 without a rotation that could tear rubber septum 32. After threads of cap 56 engage threads 88 of needle mounting collar 20, further advancement of needle assembly 46 requires relative rotation between cap 56 and needle mounting collar 20. It will be appreciated that needle mounting collar 20 is too small to be readily griped by the user of medication delivery pen 11, and is partly covered by cap 56. However, the relative rotation can be achieved by rotating body 12 of cartridge retainer assembly 10. In particular, as noted above, anti-rotation projections 76 of needle mounting collar 20 are engaged in anti-rotation slots 62 which are defined between adjacent supports 60 of body 12. Hence, rotation of body 12 is transmitted to needle mounting collar 20 and enables complete rotational engagement of needle assembly 46.

Use of medication delivery pen 11 proceeds in a conventional manner with dosing apparatus 38. As explained above, actuation of dosing apparatus 10 causes liquid medication in cartridge 22 to be urged in a distal direction. The medication will be urged through the lumen of needle cannula 48. This distally directed liquid pressure also will cause septum 32 to distend in a distal direction. However, as noted above and as shown in FIG. 7, septum 32 is spaced proximally from cork 54 of needle assembly 46, and will not be urged into contact with cork 54. Thus, the drooling or weeping of liquid medication can be substantially prevented. This is enabled because cartridge 22 is supported and accurately positioned by engagement of vial shoulder 28 with supports 60 of body 12. Hence neck 30 and crimped metallic sleeve 34 need not be closely engaged by needle mounting collar 20.

After medication delivery pen 11 has been used, needle assembly 46 is separated from needle mounting collar 20 and discarded. The user is encouraged to apply a disinfectant to the distal end of medication delivery pen 11. Disinfectants have the potential of adversely affecting some plastic materials that could be used in a medication delivery pen. However, the two-part construction of vial retainer assembly 10 enables needle mounting collar 20 to be made from a metal or other material that is resistant to disinfectants that may be applied by the user.

What is claimed is:

1. A cartridge retainer assembly for retaining a medication cartridge having a barrel and a neck, said cartridge retainer assembly comprising:

a generally tubular body having opposed proximal and distal ends and being dimensioned for securely receiving a barrel of a cartridge therein;

a generally tubular needle mounting collar having opposed proximal and distal ends and being dimensioned for receiving a neck of the cartridge therein; and

cooperating engagiment means on said needle mounting collar and said tubular body for preventing distal and proximal movement of said needle mounting collar with respect to said body and for providing transversely floatable engagement between said needle mounting collar and said body, whereby said engagement means enables said cartridge retainer assembly to accommodate dimensional variations and eccentricities of the cartridge when the neck of the cartridge is being inserted through said body and into said needle mounting collar.

2. The cartridge retainer assembly of claim 1, wherein said engagement means comprises a plurality of resiliently deflectable fingers on said needle mounting collar.

3. The cartridge retainer assembly of claim 2, wherein each of said resiliently deflectable fingers has a locking ridge thereon and wherein said engagement means further comprises a groove on said body engaging said locking ridges, said engagement of said locking ridges and said groove retain said needle mounting collar and said body in substantially fixed axial position relative to one another.

4. The cartridge retainer assembly of claim 1, wherein the engagement means of said needle mounting collar and said body further comprises means for preventing relative rotation between said needle mounting collar and said body.

5. The cartridge retainer assembly of claim 1, wherein said needle mounting collar and said body are formed from dissimilar materials.

6. The cartridge retainer assembly of claim 1, wherein said needle mounting collar comprises an array of external threads thereon for threadedly and releasably engaging a needle assembly, said threads on said needle mounting collar being disposed proximally of said distal end of said needle mounting collar.

7. A cartridge retainer assembly for retaining a medication cartridge having a barrel and a neck defining a smaller cross-section than the barrel, said cartridge retainer assembly comprising:

a generally tubular body having opposed proximal and distal ends and a chamber therebetween, said chamber being dimensioned and configured for engaging a barrel of a cartridge therein, said body further including at least one inwardly projecting support defining a distal end of said chamber and including at least one anti-rotation slot formed therein, and a annular rib spaced distally from said support and defining a locking groove therebetween;

a generally tubular needle mounting collar having opposed proximal and distal ends, said proximal end of said collar including at least one axially aligned anti-

rotation projection engaged in said at least one slot for preventing rotation between said needle mounting collar and said body, an outwardly projecting locking ridge engaged in said locking groove of said body for preventing distal and proximal movement of said needle mounting collar with respect to said body, and a plurality of resiliently deflectable fingers defined by a corresponding plurality of axially aligned slots extending from said proximal end to a location intermediate said ends, said grooves permitting deflection of said fingers to accommodate dimensional inconsistencies and eccentricities of a barrel and a neck of the cartridge.

8. The cartridge retainer assembly of claim 7, wherein said body is formed from a transparent plastic material and wherein said needle mounting collar is formed from a metallic material.

9. The cartridge retainer assembly of claim 7, wherein said plurality of slots on said needle mounting collar includes four slots extending into said proximal end and defining four resiliently deflectable fingers, said needle mounting collar further including said at least one anti-rotation projection comprising four anti-rotation projections disposed respectively at central positions on each said resiliently deflectable finger.

* * * * *

EXHIBIT 16

US005554125A

United States Patent [19]

Reynolds

[11] Patent Number: 5,554,125

[45] Date of Patent: Sep. 10, 1996

[54] **PREFILLED VIAL SYRINGE**

[76] Inventor: **David L. Reynolds**, 305 Knowlton Road, P.O. Box 600, (Knowlton) Lac Brome, Quebec, Canada, J0E 1V0

[21] Appl. No.: **245,132**

[22] Filed: **May 17, 1994**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 791,399, Nov. 16, 1991, Pat. No. 5,364,369, which is a continuation-in-part of Ser. No. 437,203, Nov. 16, 1989, Pat. No. 5,137,527, which is a continuation-in-part of Ser. No. 72,015, Jul. 8, 1987, Pat. No. 4,886,495.

[30] **Foreign Application Priority Data**

Nov. 14, 1990 [GB] United Kingdom 9024710
May 17, 1993 [GB] United Kingdom 9310084

[51] **Int. Cl.**[6] **A61M 5/00**

[52] **U.S. Cl.** **604/187**; 604/200; 604/201; 604/203

[58] **Field of Search** 604/82, 87, 88, 604/89, 91, 92, 191, 187, 200, 201, 203, 204, 205, 411, 413, 414, 415, 416, 905, 232, 218, 220

[56] **References Cited**

U.S. PATENT DOCUMENTS

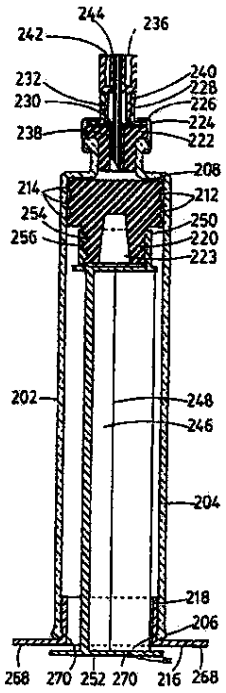
3,074,541	1/1963	Roehr	604/201
3,091,240	5/1963	McConnaughey et al.	604/218
3,699,961	10/1972	Szpur	604/89
3,811,441	5/1974	Samoff	604/218
3,967,759	7/1976	Baldwin et al.	604/218
3,976,069	8/1976	Ong	604/218
4,031,890	6/1977	Homan	604/218
4,820,272	4/1989	Palmer	604/218
4,850,966	7/1989	Grau et al.	604/82
4,861,335	8/1989	Reynolds	604/191
4,886,495	12/1989	Reynolds	604/191
5,106,372	4/1992	Ranford	604/220
5,137,511	8/1992	Reynolds	604/191
5,281,198	1/1994	Haber et al.	604/191
5,334,162	8/1994	Harris	604/88
5,352,036	10/1994	Haber et al.	604/82
5,354,284	10/1994	Haber et al.	604/232
5,364,369	11/1994	Reynolds	604/191
5,374,249	12/1994	Haber et al.	604/82

Primary Examiner—Corrine M. Maglione
Assistant Examiner—N. Kent Gring

[57] **ABSTRACT**

A prefilled syringe for one or two component medicaments is based upon the use of a vial containing a medicament or one component of a medicament, the vial having an open bottom closed by a piston. When a flexible extension of the piston is coupled with a tubular plunger, and an adaptor cap having an internal needle and an external connection for a needle is placed over a cap of the vial, the latter is converted into a prefilled syringe. The open bottom of the vial is configured so as not to interfere with handling of the vials by conventional vial sterilizing, filling and capping machinery, and may be formed so as to provide an internal shoulder which will secure a piston retention member.

14 Claims, 9 Drawing Sheets



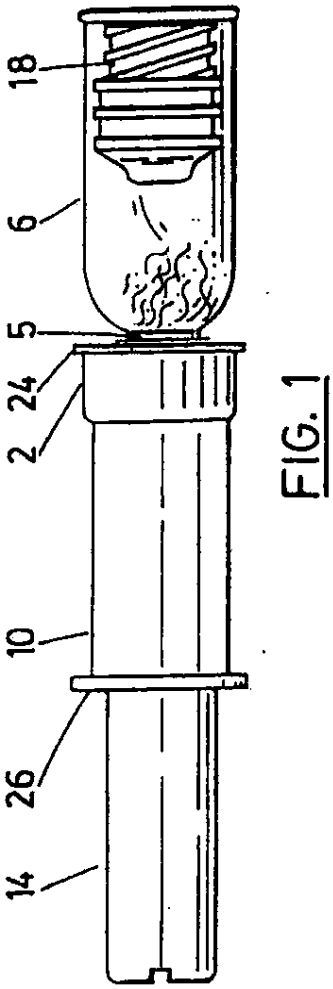


FIG. 1

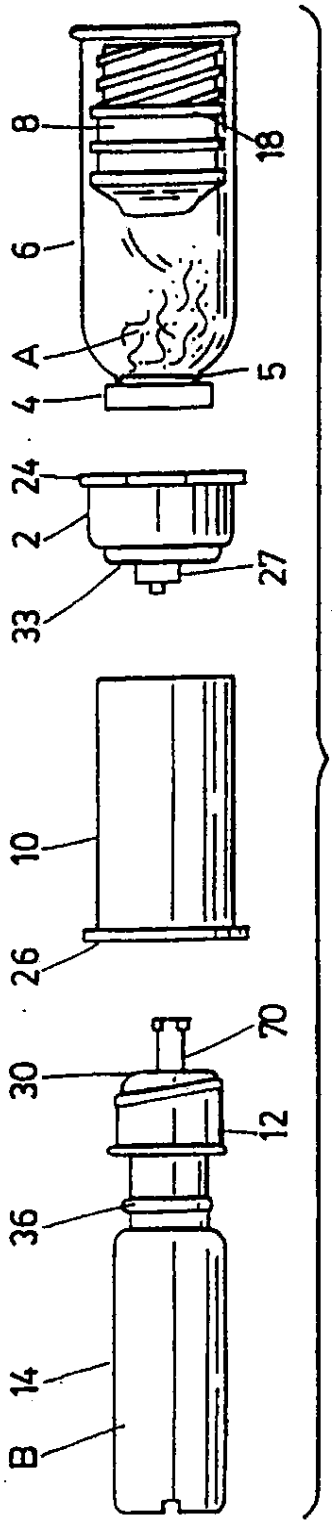


FIG. 2

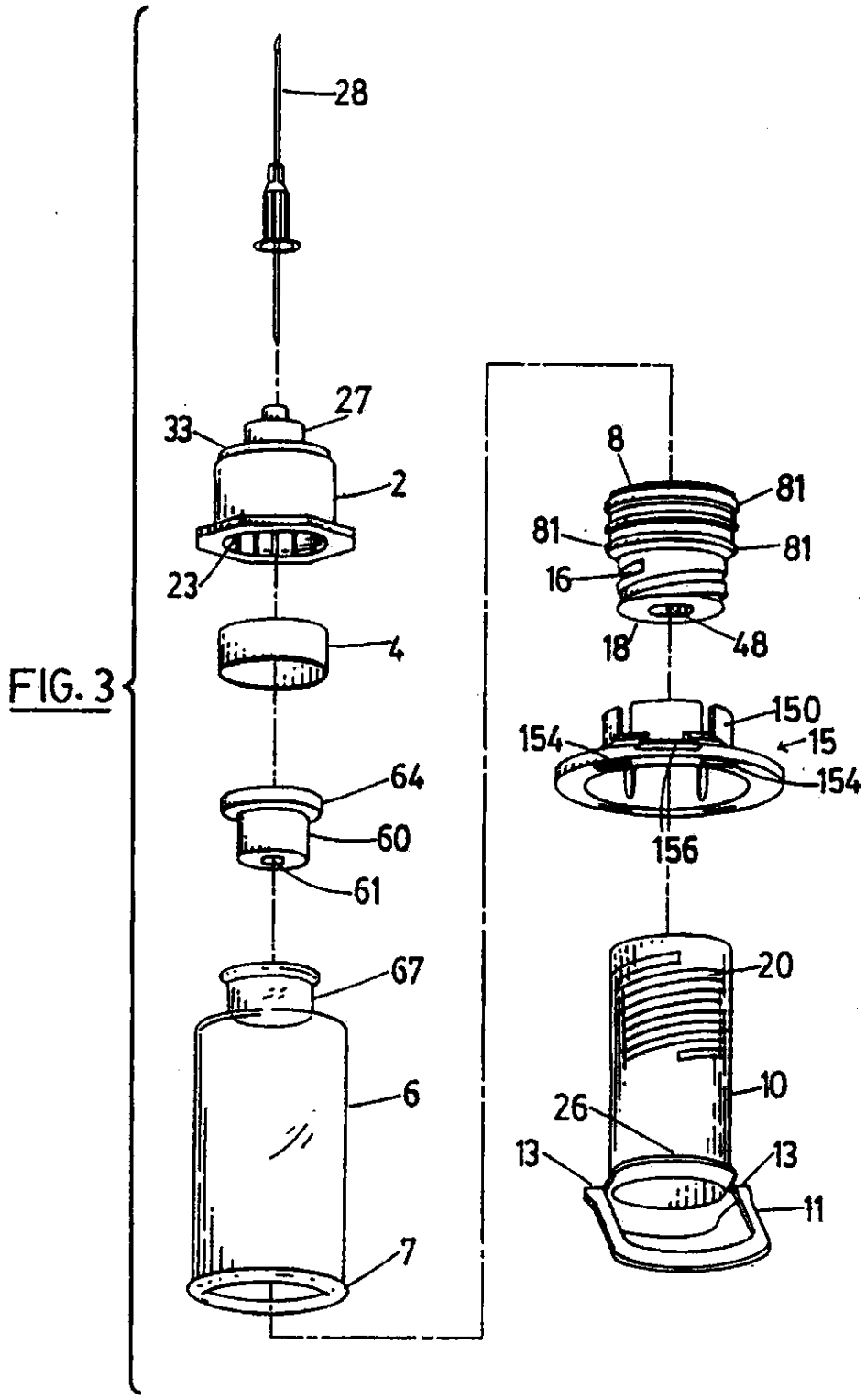

28
27
33
2
23
4
64
60
61
67
6
7
8
81
81
81
16
18
48
150
154
15
154
156
20
10
26
13
13
11

FIG. 3

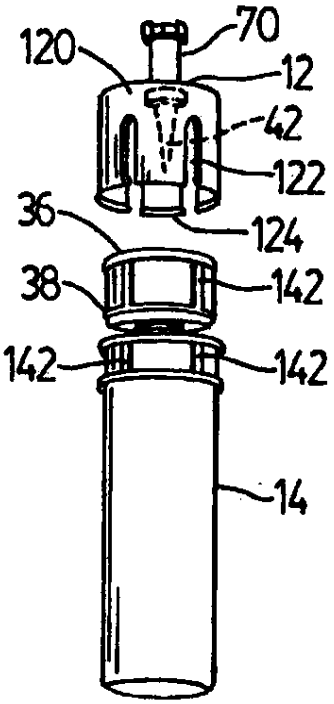

120
70
12
42
122
36
124
38
142
142
142
14

FIG. 4

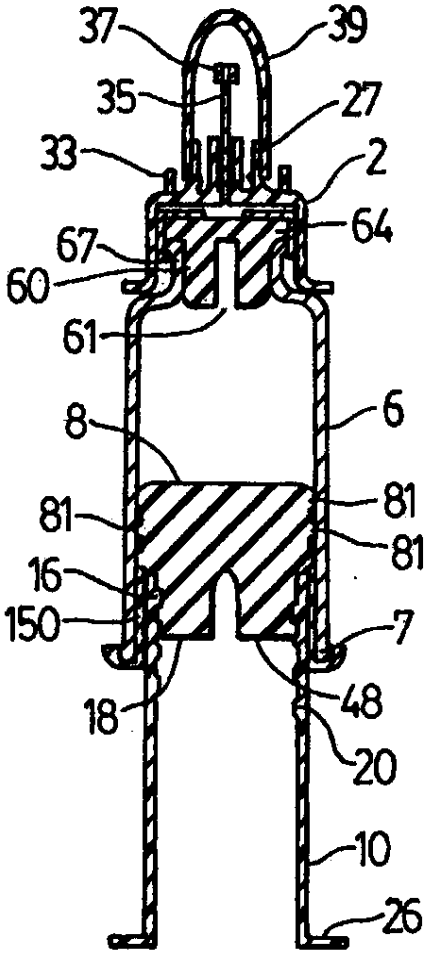

37
39
35
27
33
2
64
67
60
61
8
6
81
81
81
16
150
7
18
48
20
10
26

FIG. 5

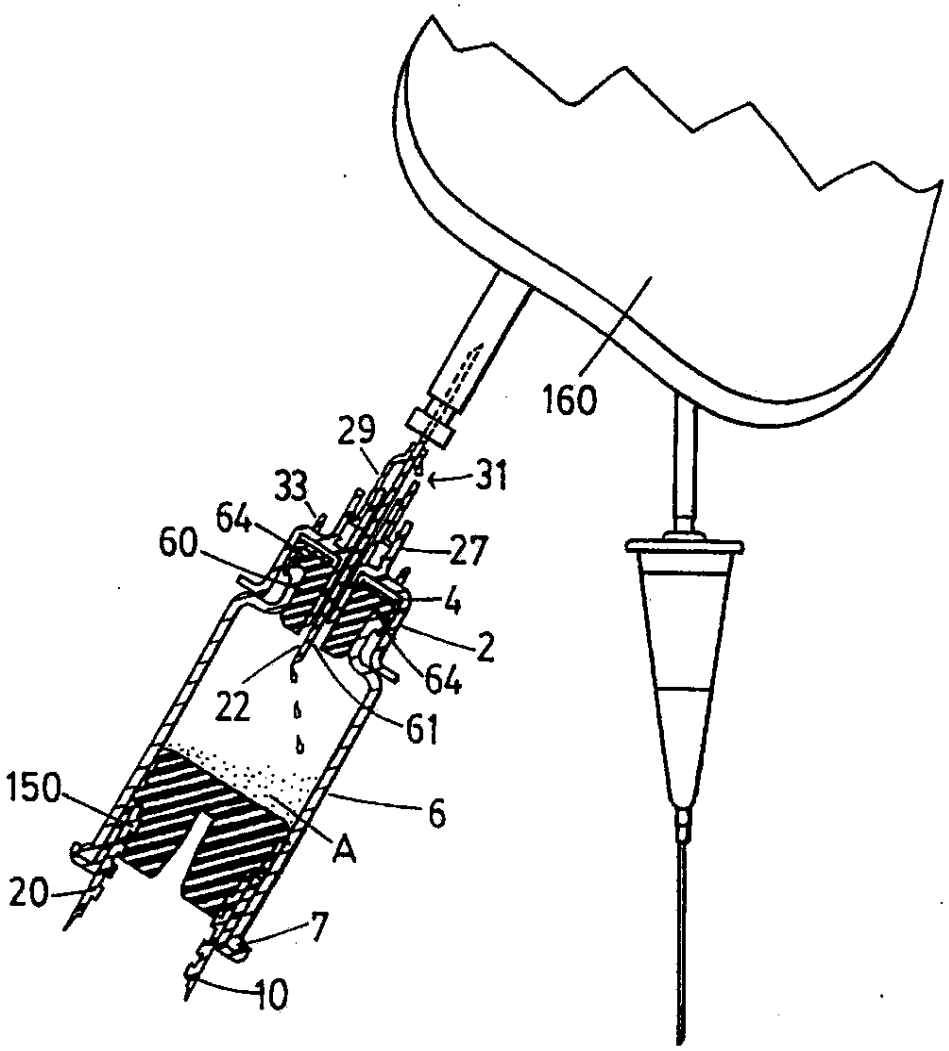


FIG. 6

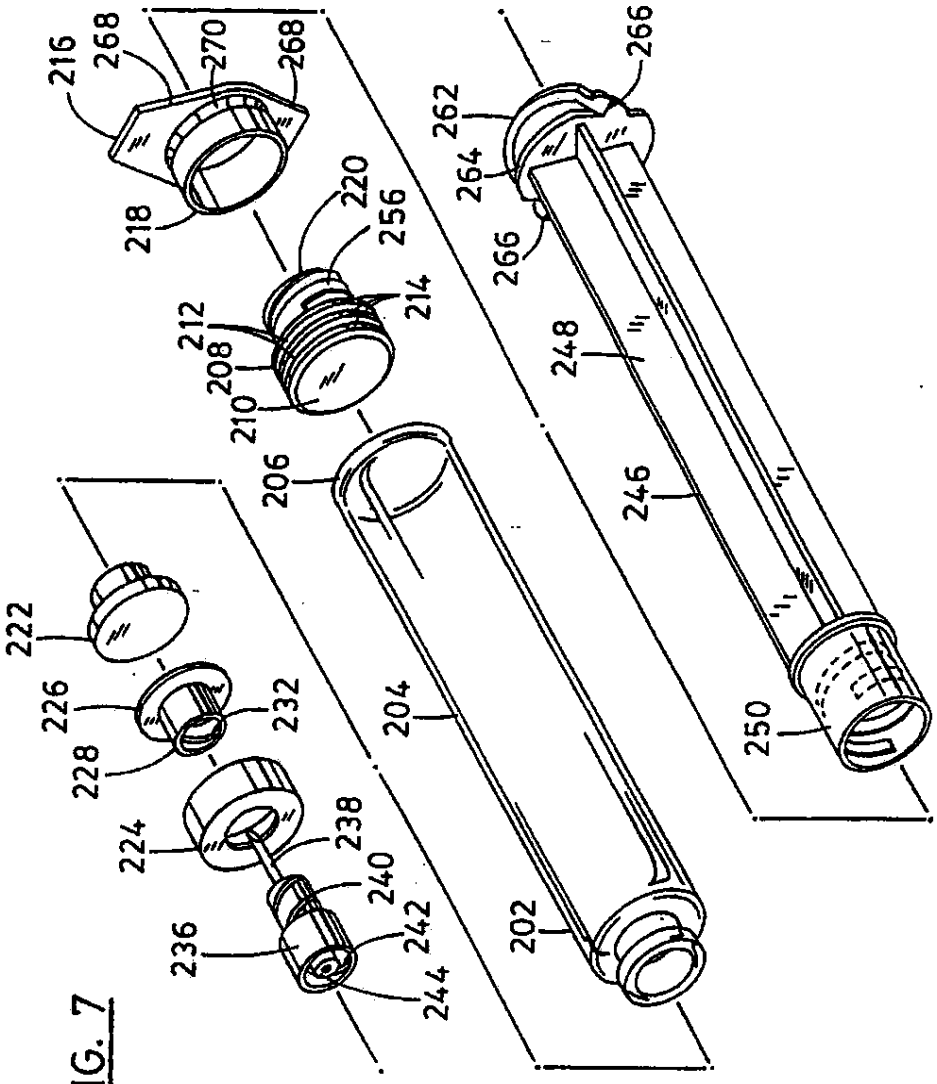

216
268
270
268
218
220
256
214
212
208
210
206
222
226
232
228
224
238
240
242
236
244
204
202
262
264
266
266
248
246
250

FIG. 7

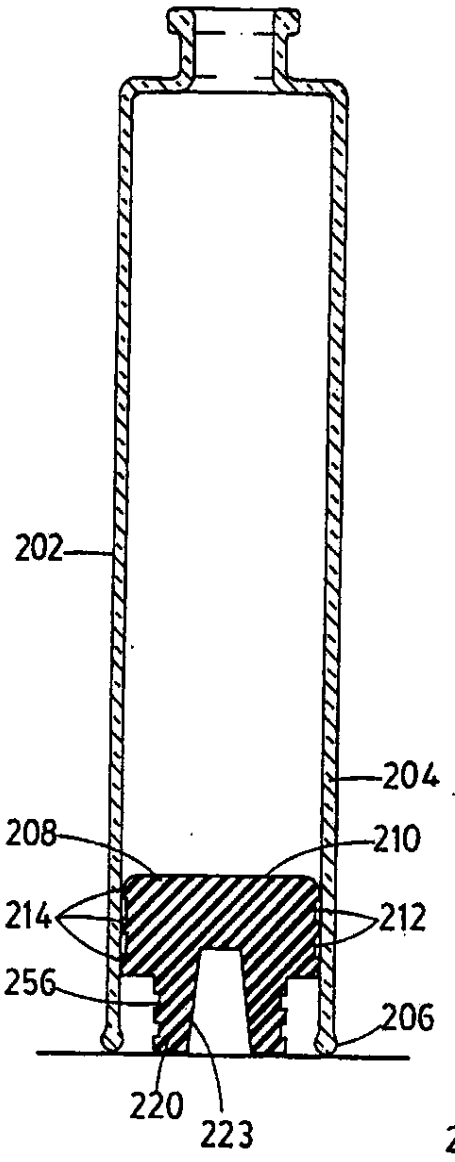

202
204
208
210
214
212
256
206
220
223

FIG. 8

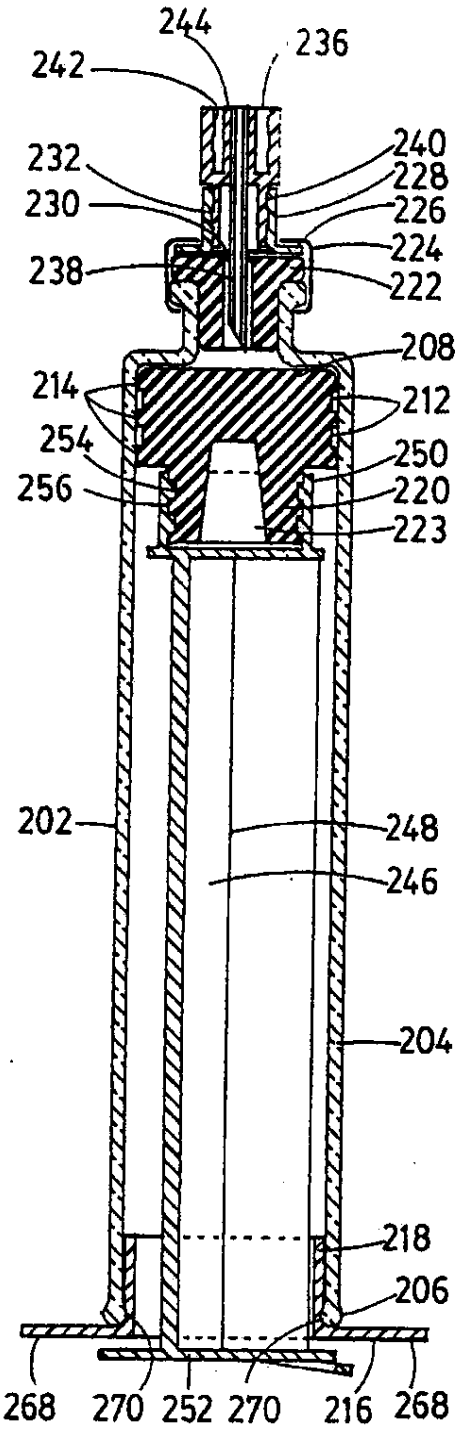

244
236
242
240
232
228
230
226
224
238
222
208
214
212
254
250
256
220
223
202
248
246
204
218
206
268
270
252
270
216
268

FIG. 9

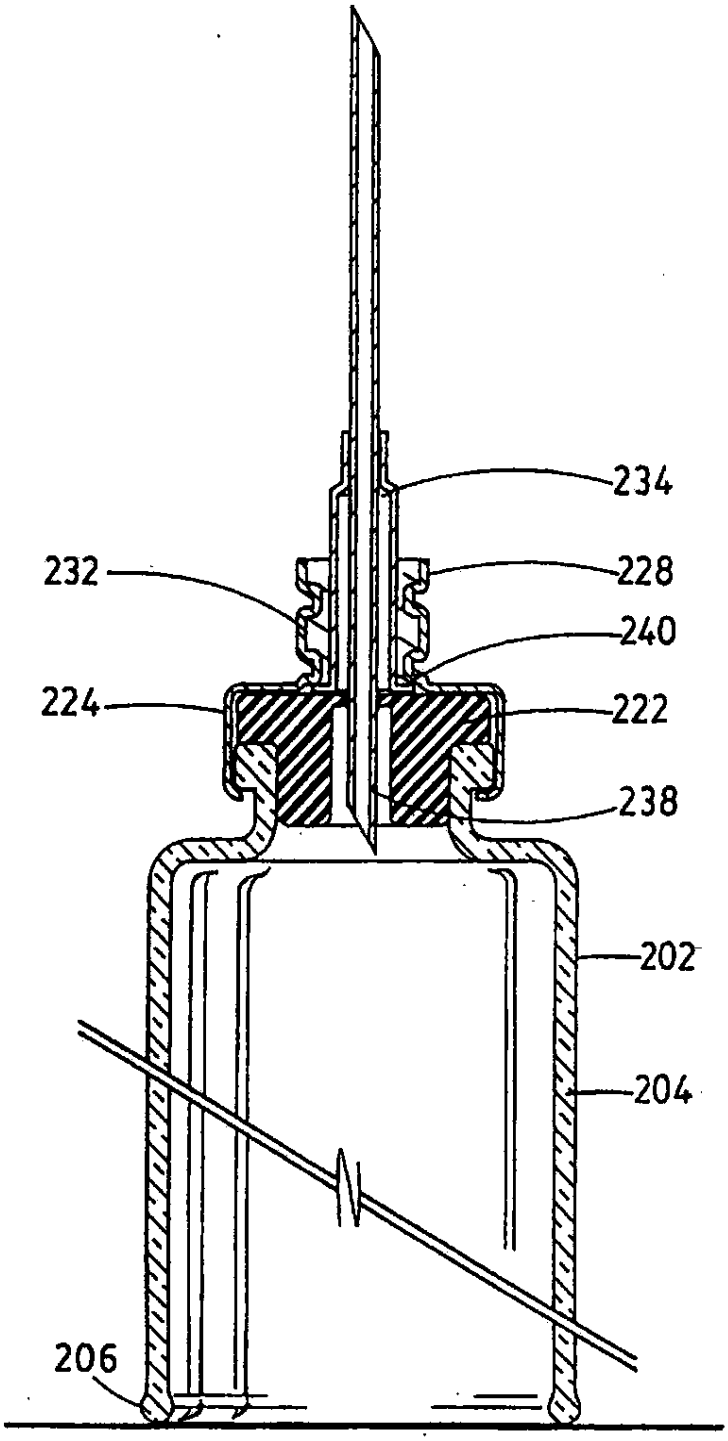


FIG. 10

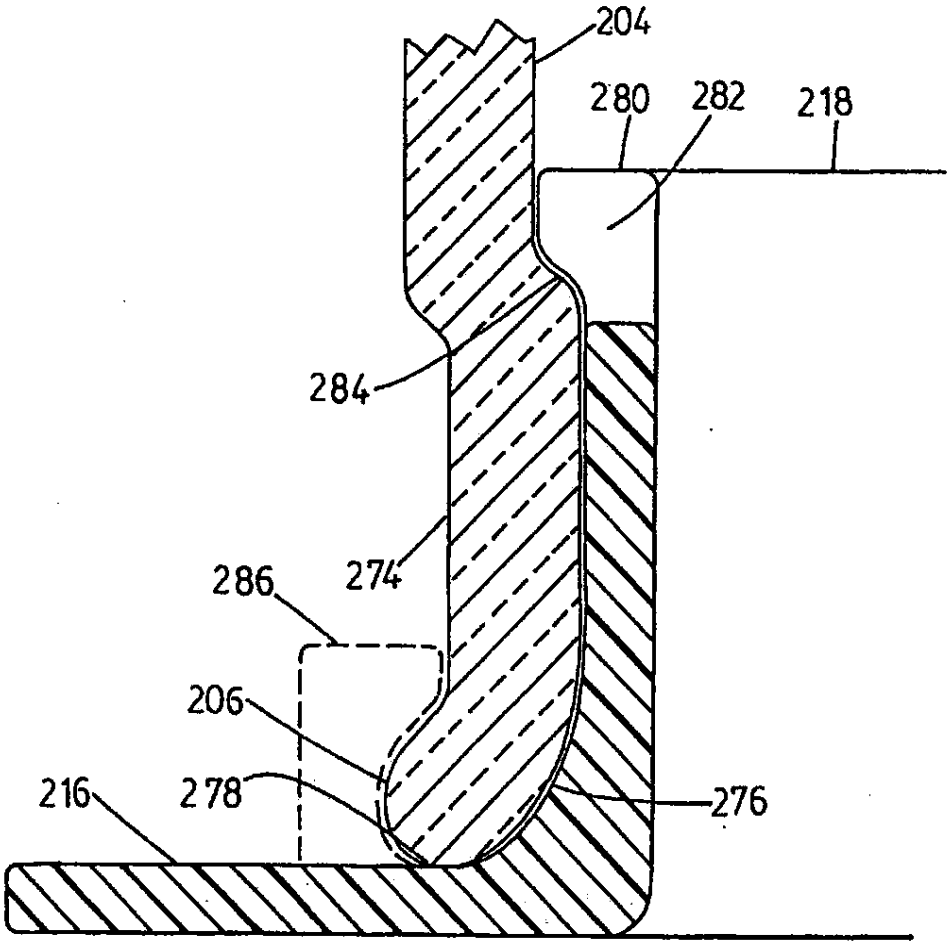


FIG. 11

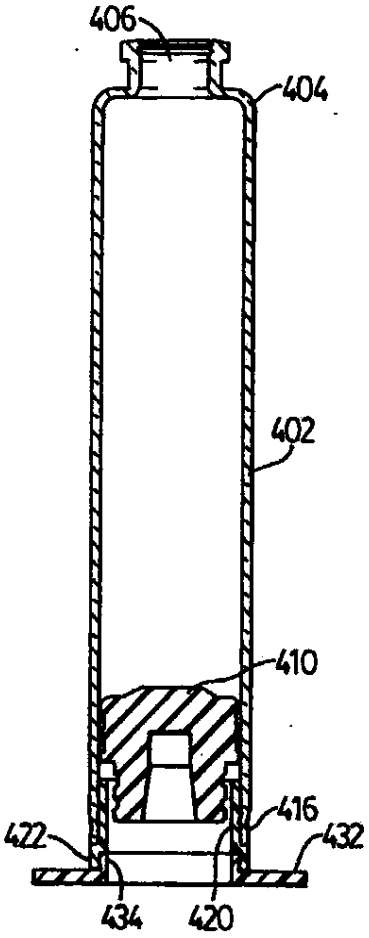

406
404
402
410
416
422
432
434
420

FIG. 12

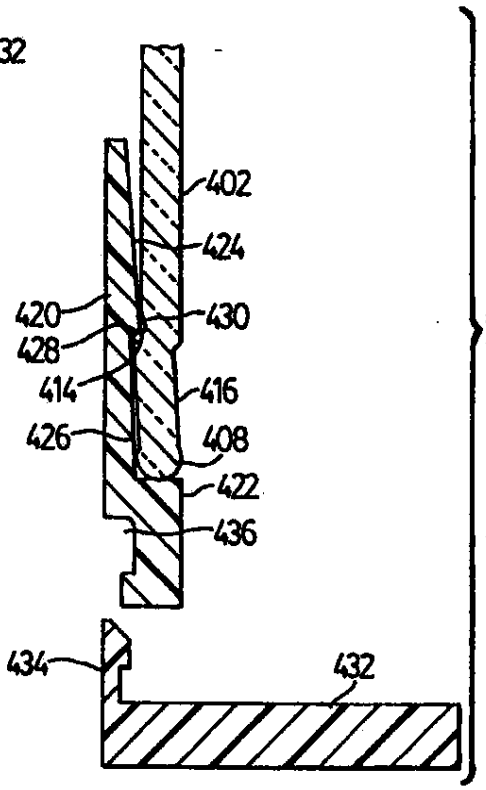

402
424
420
430
428
414
416
426
408
422
436
434
432

FIG. 13

PREFILLED VIAL SYRINGE

REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of my application Ser. No. 07/791,399 filed Nov. 16, 1991 now U.S. Pat. No. 5,364,369, which is a continuation-in-part of application Ser. No. 07/437,203 filed Nov. 16, 1989 now U.S. Pat. No. 5,137,527 which is a continuation-in-part of application Ser. No. 07/072,015 filed Jul. 8, 1987 and now U.S. Pat. No. 4,886,495.

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to prefilled syringes for use in medical or veterinary treatment.

2. Review of the Art

There has been an increasing trend in recent years to the putting up of pharmaceuticals in dosage forms so as to minimize the preparation required to administer a medicament to a patient and to reduce the chances of dosage errors or contamination. One dosage form which has been gaining rapid acceptance is the prefilled disposable syringe. Various difficulties are however associated with the preparation and usage of such syringes, particularly in the case of preparations which, in ready to use condition, have a short shelf life. Numerous forms of dual compartment syringe structures have been proposed for the shipping of such preparations with components stored in separate compartments for admixture immediately prior to use. Although certain structures have met with some degree of acceptance, they are commonly difficult to manufacture and/or use because of difficulties in filling the syringe with the components, and because they require extensive manipulation immediately prior to use. Moreover they are frequently substantially more bulky than conventional syringes because in many cases they frequently comprise components which effectively represent two syringes in tandem.

Problems in the manufacture of prefilled syringes are not confined to two component systems and even with single component systems the filling of syringes under factory conditions is difficult to mechanize effectively and requires expensive special purpose syringe filling machinery. The same applies to related units prefilled with liquids required for injection or infusion during medical procedures.

Another approach where single component systems are involved is exemplified by British Patent Specifications Nos. 1,252,306 and 1,444,119, and U. S. Pat. No. 4,445,895, in which a prefilled cartridge having a displaceable plug at one end, and a needle penetrable closure at an opposite end, is inserted into the barrel of a syringe for dispensing of its contents. Whilst such cartridges and the equipment for filling them are known and available, they are only really suitable for preparations which can be stored in liquid form, and require either a special or a modified syringe for their use. The cartridges themselves require special filling apparatus.

In a further arrangement disclosed in U.S. Pat. No. 3,845,763, a cartridge or vial is closed at its bottom end by a slidable plug with a downwardly extending stem, which cartridge or vial is inserted bottom end first into a special holder which carries a double ended needle, so that the stem is penetrated by the needle and the body of the vial is converted into a plunger which can be depressed to expel the contents of the vial through the stem. The projecting stem

means that the vial cannot be filled utilizing conventional vial filling machinery.

The high capital expenditure involved in implementing known prefilled syringe systems has severely limited their adoption to those few cases where their advantages outweigh the substantial additional unit costs involved as compared to conventional modes of delivery.

SUMMARY OF THE INVENTION

The present invention seeks to provide a system for the distribution of preparations required for injection or infusion in liquid dosage form during medical procedures, which has a wide range of utility both for single component liquid preparations or for two component systems of which one component may be a solid, which utilizes a small number of components all suitable for mass production using material already approved for usage in such applications, which is simple to assemble and can be filled utilizing equipment already available to most pharmaceutical manufacturers, which minimizes the number of "clean room" operations required, and which minimizes certification problems.

The system is based upon and built around a basic component in the form of a 'bottomless vial'. Such a bottomless vial has all of the characteristics of a conventional pharmaceutical vial, except that the glass base of the vial is replaced by a piston wholly received within the vial and designed to form a hermetic seal with its cylindrical side wall, the seal being maintained both when coupled and when uncoupled from a plunger releasably connectable to the piston for moving the latter axially of the vial. A particularly important characteristic of such a bottomless vial is that it can be conveyed, filled and capped reliably by conventional vial sterilization, filling and handling equipment such as is already possessed by most pharmaceutical manufacturers. To this end, the bottomless vial must be free of features which would significantly compromise its stability when handled by such equipment. A flange or bead is required around the base of the vial for various reasons, but must result in no more than a slight increase in the overall diameter of the vial, and must be configured so as to avoid any substantial increase in its tendency to tip when jostled by other similar vials, and the centre of gravity of the vial must not be displaced so far upwardly as to substantially reduce the stability of the vial.

I have found that it is important that the bottom end of such a bottomless vial terminates in a somewhat rounded peripheral bead, which serves several purposes. Firstly, it strengthens the open end of the vial and reduces stress concentrations and the risk of breakage, particularly during insertion of the piston, as well avoiding the danger of glass particles chipping from the edge of the glass which arises in the absence of such rounding. Secondly, the rounding produces a slight internal flare which facilitates piston insertion. Thirdly, it provides means, if sufficiently pronounced, for securely engaging a subsequently applied piston retainer which prevents possible ejection of the piston during shipping and storage of the vial due to gas generation or expansion within the hermetically sealed vial above the piston.

Whilst the provision of a pronounced bead is thus highly desirable, conventional formation of the bead as an external projection on the body has the disadvantage of increasing the diameter of the bottom of the body, thus both increasing the capability of tipping of the vials while being conveyed, and possibly providing a ramp for such tripping by riding

over or under the beads of adjacent vials unless the external configuration of the bead is carefully controlled. At the same time, particularly for syringes prefilled with a single component liquid pharmaceutical, there may be a requirement for a syringe capacity which requires the height to diameter ratio of the body to be increased as much as possible, which in turn requires maximum stability of the vial when conveyed free-standing.

The piston must be capable of maintaining a hermetic seal with the wall of the vial, of integrity comparable to that achieved during capping of a conventional vial, and this seal should be maintained in storage and during manipulation of a syringe system incorporating the vial, during which the piston may be subject to non-axial forces transmitted to it by a plunger and tending to break the seal.

In the context of the invention, it should be understood that "vial" refers to a particular type of container, having a rather squat cylindrical body whose height compared to the diameter of its base is such that it may stand stably on its base whilst being conveyed through a vial handling and filling machinery and whilst subsequently sealed and capped. Its body should also be free of external projections large enough to interact with other vials or the filling machinery in a manner such as to promote tipping. A vial has a neck with a large enough internal diameter to permit filling from a vial filling machine: solid filling materials will normally require a larger neck than liquids. Vials should not be confused with cartridges, which are comparatively long and slim, and cannot usually be filled utilizing vial filling machinery since they are too tall to rest in a stable manner on their bases. Cartridges also are typically thin-walled and lack a bead or flange, which renders them fragile, and makes it difficult to insert a piston without excessive risk of breakage.

The differences between such vials and a conventional vial do not prevent them from being filled and capped in conventional vial filling and capping machinery; indeed, apart from the replacement of the bottom wall of the vial by a piston as specified, it is a conventional vial, and can be handled normally by the machinery during filling with either liquid or solid material. The presence of the piston, which is relatively massive, in the lower part of the vial even helps stabilize the latter during filling. Obviously the cubic capacity of such a vial is less than the capacity of a conventional vial of comparable overall dimensions but for most purposes this is immaterial.

The invention provides in one aspect a pharmaceutical vial used for forming a barrel and a piston of a syringe after being filled and capped, comprising a cylindrical glass vial body having at one end an integral open neck and a peripheral external flange around an outer end of the neck, a peripheral rounded edge defining an inner periphery of an open opposite end, and a piston of resilient material having a cylindrical head within and concentric with the cylindrical glass body, the piston maintaining a slidable hermetically sealing relationship with a main inner cylindrical surface of the body, and being located to define a chamber of volume equal to the nominal capacity of the vial between the piston head and the neck of the vial, the piston having integral coupling structure wholly within the body for subsequent connection to a syringe plunger, and the vial being stable when standing on the open end of the body such that it can be conveyed while so standing through vial filling and capping machinery without tipping over, the body being formed adjacent said open end with peripheral radially extending positive retention means for engagement with complementary configurations of a tubular piston retaining member subsequently inserted within said open end of the body to resist overpressure within the body, wherein the retention means is formed by shaping a lower end portion of the body to have a reduced internal diameter such that the retention means is formed by an upwardly facing shoulder at the top of the lower end portion which projects inwardly of the projected circumference of said main interior cylindrical surface, and the lower end portion is located essentially within the projected circumference of a main cylindrical external surface of the body such as to leave the external surface of the body free of projections having an adverse effect on the stability of the vial.

A vial in accordance with the invention may be converted into a syringe by the addition of a plunger coupled to the piston and an outer cap which acts as a needle carrier. More specifically, the syringe includes as well as the vial a syringe plunger connected to the flexible extension from the piston, and an outer cap engaged over the cap of the vial, the outer cap having a hollow needle projecting axially within the cap and a coupling for engagement with injection means and communicating with said hollow needle, the outer cap being axially movable relative to said cap of the vial from a position in which the needle ends short of the cap of the vial to a position in which it penetrates the cap of the vial. The plunger is provided with radially extending flanges for sustaining actuating forces applied to the syringe through a flange grip provided on the outer cap or on a plunger guide or piston stabilizer ring applied to the open end of the vial.

In a syringe for a two component medicament, it is necessary to provide for packaging of the second component and its admixture with the first component in the vial prior to dispensing. The invention thus further extends to a capsule assembly comprising a generally cylindrical sealed capsule having walls formed of a flexible needle penetrable material of suitable properties, a generally cylindrical neck defined by said walls at one end of the capsule, said neck having axially spaced inner and outer peripheral ridges, and a generally cylindrical cap applied to said neck so that a detent within the cap engages the outer peripheral ridge on the neck, a hollow cannula being formed integral with and passing through said cap so that an inner penetrating end within the cap ends short of the neck of the capsule and an outer end in the form of a fluid coupling which extends outwardly of the cap, the cap being displaceable relative to the capsule to a position in which the detent rides over the inner ridge and the inner end of the needle penetrates the neck of the capsule, the cap and capsule being of a diameter such that they can enter the tubular plunger to a position in which a coupling at the outer end of the cannula, is connected to the coupling on the outer cap of the syringe, with the plunger being used as a support for the capsule prior to being coupled to the piston.

Thus the injection system comprises a sequence of components of which various sub-sequences can be combined to form injection systems for preparations requiring shipping and storage as two separate components, certain sub-sequences themselves having utility respectively as injection systems for single component liquid preparations. "Injection" is utilized broadly to cover hypodermic, intramuscular and intravenous injection, gravity and mechanical infusion, and injection into other vessels utilized in medical treatment or testing. For the purposes of description, the "front" or "top" end of an injection system will be considered the end of the system from which a liquid preparation is so injected.

The invention also provides, in a method of producing a prefilled syringe for administering a pharmaceutical preparation, said syringe comprising a generally cylindrical

syringe body having a neck at one end and a side wall having a bead finish at the other end, at least a component of the preparation filled into said body, an elastomeric closure closing the body at the neck end and secured by a cap, and an elastomeric piston at said other end forming a hermetic seal with an inside surface of said side wall, needle means for movement relative to the cap to penetrate the elastomeric closure, and plunger means for connection to an outer side of the piston, the improvement wherein the syringe is produced by associating components, including said plunger and said needle, with a prefilled vial produced by forming said body with height to diameter ratio such that the body is stable, and so that any outward extent of the bead is insufficient to result in interference such as would cause tipping, when the body is conveyed standing on said other end through equipment for filling and capping pharmaceutical vials, inserting said elastomeric piston wholly within said other end of the body to form a vial open at the neck, and filling said vial through said neck with said pharmaceutical preparation component, and then applying said elastomeric closure on said cap, whilst conveying the vial standing on said other end through equipment for filling and capping pharmaceutical vials.

Further features of the invention will become apparent from the following description of preferred embodiments thereof with reference to the accompanying drawings.

SHORT DESCRIPTION OF THE DRAWINGS

FIGS. **1** and **2** are elevational and exploded views of a first embodiment of the syringe system;

FIG. **3** shows the separated parts of a modified embodiment of the syringe system;

FIG. **4** shows, separated, a diluent capsule and cap for use with the system of FIGS. **1** and **2** or **3**;

FIG. **5** is a longitudinal cross section through the assembled system of FIGS. **3** and **4**;

FIG. **6** is a fragmentary view of a syringe in accordance with the invention utilized in conjunction with an I.V. bag;

FIG. **7** is an exploded isometric view of the components of a further embodiment of syringe;

FIG. **8** is a vertical section through a vial portion of the syringe of FIG. **7**, ready for filling;

FIG. **9** is a longitudinal section through an assembled syringe, after discharge of its contents;

FIG. **10** is a fragmentary longitudinal section on an enlarged scale of a portion of the syringe shown in FIG. **9**, showing a modification of the arrangement shown in that Figure; and

FIG. **11** is an enlarged vertical section through the bead of a modified embodiment of the syringe, also showing adjacent parts of a modified piston retainer and finger grip.

FIG. **12** is a longitudinal section through the body of a further embodiment of bottomless vial, shown fitted with a piston retainer ring;

FIG. **13** is a detail of the body and retainer ring shown in FIG. **12**, on an enlarged scale;

DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring to FIGS. **1** and **2**, a syringe system for the injection of a liquid preparation stored as two components comprises seven primary mechanical components, apart from the components of the preparation. The components of the preparation typically comprise a first component A which may be in any physical state suitable for storage in vial, and a second liquid component B, typically but not necessarily sterile water. The liquid component B is stored in a sealed capsule **14** of flexible material, manufactured using conventional techniques from a material, usually synthetic plastic, which is compatible with the contents of the capsule. The first component is stored in a cylindrical vial **6**, typically of glass, and capped by an annular cap **4** which retains a conventional needle penetrable sealing member accessible through a central opening in the cap. By a vial is meant a cylindrical vessel which can assume a stable upright position supported by its base, the overall height of the vessel exceeding the external diameter of the rim of its base by a factor sufficiently small that it remains stable when passing through conventional vial filling and capping equipment utilized to fill and cap the vial. This factor preferably does not exceed 2.5 for the present embodiment, but can be increased by means discussed further with reference to FIGS. **7–13**. A neck **5** at the upper end of the vial **6**, which is capped by the cap **4**, has a relatively internal diameter characteristic of such vessels, usually not less than about 7.5 mm for liquid or 10 mm for solids, so that filling with either liquids or solids can be readily achieved. The cap **4** is formed by an aluminum sleeve, having a flange retaining a sealing member formed by a soft rubber disc or plug **5** over or in the front end opening, and tightly crimped onto a neck at the front end of the vial so as to seal the latter. A major difference from conventional vials is that the conventional bottom wall of the vial is replaced by an axially movable piston **8** wholly within the vial and in sealing contact with the vial walls. When received within the vial **6**, this piston in no way interferes with the handling of the vial using conventional machinery, and in particular permits the vial to be stood on its base with its neck (**5**) (which forms the front end of the vial when in use) upwards as it passes through the filling and capping equipment.

The filled vial **6** may be converted into a prefilled syringe by applying an outer cap **2** over the cap **4** and positively attaching a cylindrical plunger sleeve **10** to the piston **8**. The piston **8**, typically formed of rubber, is moulded with a rearward extension **16** with an external thread **18**, while the interior of the front end of the plunger sleeve **10** is formed with a complementary internal thread **20** (see FIG. **3**) so that it may be screwed onto the piston **8**. A recess **48** (see FIG. **3**) may be formed in the extension **16** to increase its flexibility. The outer cap **2** fits over the inner cap **4** so that a hollow needle **22** (see FIG. **6**) formed within the cap **2** does not reach the penetrable zone of the cap **4**. On the front of the cap **2** and in communication with the hollow needle **2** is a coupling adapter **27**, for example similar to those sold under the trade mark LUER-LOK, for connection of the syringe to a needle **28** or other instrumentality (see FIG. **3**). To prepare the syringe for use, the outer cap **2** is pulled back over the inner cap **4** so that the needle **22** penetrates the cap, and the needle **28** or other instrumentality is applied. This should be done without pressing on the plunger sleeve so as to avoid accidental ejection of the contents of the syringe. The rear ends of both cap **2** and the sleeve **10** are formed with radially extending flanges **24** and **26** respectively which form finger grips for operation of the syringe. Thus if a user grips the assembled syringe by the flanges and presses them towards each other, the contents of the syringe can be expelled through the needle **22** and the needle **28**. It will be noted that the rear end of the vial **6** is formed with only a relatively slight external bead **7** rather than the wide finger flange commonly found on the barrels of conventional

syringes. In the present arrangement, the flange 24 provides the function of such a finger flange, enabling the bead 7 to be reduced to a size which will avoid such interference between the flanges of adjacent vials as would cause tipping when the vials are conveyed in a vertical attitude through filling and capping equipment.

In many applications, it is desirable to prevent premature penetration of the plug 5 by the needle 22, and therefore the cap 2 may be moulded with short internal threads (not shown) which prevent rearward movement of the cap 2 unless it is twisted so that the threads bite into the soft aluminum of the cap 4 and draw the cap 2 rearwardly so that the needle 22 can penetrate the plug.

A prefilled syringe constructed as discussed above has significant advantages over conventional prefilled syringes in that the vial may be filled using conventional vial filling equipment, and yet may be utilized directly instead of requiring its contents to be transferred to a syringe prior to use as has been conventional in the use of vials.

The vial may also be charged with material which is not directly injectable, such as solids which must be dissolved or suspended in a liquid medium prior to injection. In this case the liquid medium is sealed as already described in a flexible capsule 14. A third cap 12 is applied to the capsule as shown in FIG. 2, which is inserted into the plunger sleeve 10 so that a screw thread 30 on the exterior of the cap engages screw thread 20 within the sleeve.

A neck 34 of the capsule 14 (see FIG. 4) has two peripheral ridges 36 and 38. As the cap 12 is applied to the capsule, a detent 40 within the cap is pushed over only the outer ridge 38 so that a hollow needle 42 mounted in the cap stops short of the end of the capsule. By forcing the detent 40 rearwardly over the ridge 36, the needle 42 can be forced rearwardly so as to penetrate the capsule.

The conduit in the needle 42 extends through the cap 12 into an extension 70 which is configured at its outer end to couple with a standard syringe coupling such as the coupling 27 on the cap 2. This enables the capsule 14, once inserted in the plunger 10, to be locked through the extension 70 and the coupling 27 to the cap 2 to produce the compact assembly shown in FIG. 1. The inner end of the plunger 10 is a press fit on an annular retaining flange 33 formed on the cap 2. To prepare the syringe for use, the cap 2 is forced rearwardly over the cap 4 so that the needle 22 within the cap 2 pierces the seal 5, and the capsule 14 is forced forward so that it is pierced by the needle 42 and its contents can be expelled through the needle 42, the extension 70, the coupling 27 and the needle 22 into the vial 6. The assembly of the capsule 14 and the plunger 10 can then be released from the remainder of the syringe by turning so as to release the extension 70 from the coupling 27, a needle (see FIG. 3) may be applied to the coupling 27, the capsule 14 is removed from the plunger 11 and discarded, and the plunger 11 is screwed onto the coupling 18 to ready the syringe for use.

A similar arrangement may be utilized for single component medicaments in which case the capsule 14 and cap 12 are not provided. The arrangement is advantageous for both single and multiple component medicaments since only the vial need be assembled and filled in a clean room, the only additional step required over the filling of a conventional vial being the insertion of the piston 8. The plunger 10 may be pressed onto the cap 2, and this assembly, if desired together with a needle and/or a capsule 12 and cap 14, may be separately sterilized and packaged, without endangering the stability or destroying the contents of the vial, which will often be sensitive to heat or radiation utilized for sterilization purposes. Since the capsule 12 can withstand conventional terminal sterilization techniques (see further below), it can be sterilized independently of the vial. This is a major advantage over many two-component syringe systems in which the components are separated only by some form of penetrable plug or diaphragm and must therefore either be fully assembled in a clean room, or subjected in assembled form to terminal sterilization techniques which may destroy or damage a component of the pharmaceutical preparation.

Where the capsule 12 is not being used, it is possible to utilize a cap 2 in which the needle 22 is not provided, and instead use a needle arrangement as shown in FIG. 3 or FIG. 5.

Further features of the invention are shown in FIGS. 3–5. The same reference numerals are used to denote the same parts in these figures as in the previous figures, where applicable, and construction and operation are similar except where otherwise indicated.

FIGS. 3–5 show a vial and syringe system according to the invention, the vial comprising a body 6 of rigid transparent material, usually glass although synthetic plastic resins might be utilized in certain applications. The body has the general configuration of a conventional vial except for the absence of a bottom wall. In order to compensate for the strengthening effect which would be provided by the bottom wall, in order to provide a detent for an optional plunger stabilizer ring 15 described further below, and in order to permit a slight flare at the extreme bottom end of the vial, a rounded bead 7 is provided around the perimeter of the bottom end of the body, although its peripheral extent should not be sufficient to increase substantially the diameter of the vial or decrease substantially its stability during handling.

A medicament A is retained within the vial by a piston 8. A closure 60 substantially fills a neck portion 67 of the vial after the vial, closed at the bottom by the piston, has been filled through its neck portion by a conventional vial filling machine. Although the medicament shown is a solid, it may be a liquid, or filled as a liquid and lyophilized to leave a solid residue. The piston 8 is moulded from rubber, preferably of at least 50 durometer hardness, and is formed with multiple, preferable three, peripheral ribs 81 on its outer surface, the external diameter of the ribs being slightly greater than the internal diameter of the body 6 so that an hermetic seal is established when the piston is pressed into the bottom of the body, initial entry being assisted by the flare mentioned above. The piston is moulded as a substantially solid body so that it has sufficient rigidity to maintain the desired hermetic seal with the body, any central bores within the piston (see FIG. 5) required to assist needle penetration being of insufficient radial extent to have any significant effect on its rigidity. Although in the piston shown in FIG. 6, a central bore 48 does just extend into the piston proper, its axial extent within the piston and its diameter are sufficiently small relative to the piston diameter that the rigidity of the piston is not substantially reduced.

The piston has a downward extension 18 of reduced diameter, in which the bore 48 is also present. The diameter of the bore 48 forms in this case a greater portion of the diameter of the extension 18, whose flexibility is thus somewhat increased by its presence. The extension carries on its outer surface a multistart thread, defined by grooves 16 which terminate abruptly short of the piston, forming abutments serving a purpose discussed further below. Provided that the hardness and rigidity requirements for the piston as a whole are met, the rubber utilized to form the piston, and any external coating on the rubber (which may

act to increase the effective hardness of the rubber), are selected for compatibility with the medicament contained in the syringe, a number of approved materials being available and well known in the pharmaceutical art.

The neck closure **60** may be formed of similar rubber. After insertion of the closure **60**, its flange **64** may be held in place by a conventional cap **4** crimped over the flange and a flange on the neck of the bottle. Such a cap **4** may have a flip-off top attached to a separable central portion of the cap, partially severed from the remainder of the cap so that these portions may be broken away prior to assembly of the syringe to expose a central needle penetrable zone of the closure **60** above the bore **61**.

The piston together with its extension **18** is relatively massive, with a weight which typically amounts to at least a major portion of that of the body **6**. This weight in the lower part of the body assists in stabilising the vial during handling and filling and further inhibits tipping.

As mentioned above, vial assembly and filling will normally be performed in a clean room, since many pharmaceuticals will not withstand terminal sterilization procedures. The only additional step which requires to be carried out in the clean room other than is conventional in the filling of vials is the insertion of the piston **8**.

In order to convert the basic vial into a syringe system, the procedure described with reference to FIGS. **1** and **2** may be used. Only the differences will be described in detail for this embodiment. FIG. **3** shows the components of a syringe system separated, while FIG. **5** shows them assembled and sectioned (although an alternative needle arrangement is shown in FIG. **5**). It should be understood that the diluent cartridge **14** and cartridge cap **12** as shown in FIG. **4** are optional features of the system and will only be utilized when a diluent or solvent is required for the content of the vial which is not provided by some other means.

Referring to FIGS. **3** and **5**, an outer cap **2** is pushed over the cap **4**, and is similar to that shown in FIG. **2**, except that the internal needle **22** shown in FIG. **6** is omitted, the syringe being utilized with an alternative needle arrangement. In FIG. **13**, a conventional double ended needle **28**, is shown, the inner end of which replaces the needle **22**.

FIG. **5** shows an arrangement in which the needle **28** may be single ended, an auxiliary hollow needle **35** being provided with a cylindrical sleeve **37** at the top which replaces the outer extremity of the inner portion of the coupling **27**. A cap **39** is provided to retain the needle **35** within the coupling **27** until the needle **28** is fitted. When the syringe is to be used, the cap **39** is removed, and the sleeve of the needle is placed over the sleeve **37** and pushed down so that the needle **35** can penetrate the top of the vial and the needle **28** can be engaged with the coupling **27**.

These needle arrangements are preferred for a syringe which is shipped in an essentially ready-to-use form, since the cap **2** may be pushed fully onto the cap **4** during assembly, yet the closure **60** remains unpenetrated until the needle (or other instrumentality as discussed below) is fitted at the time of use. On the other hand, the integral needle **22** is convenient where the assembly is to be utilized in the manner shown in FIGS. **1** and **2** and a capsule **12** is utilized. The inner surface of the cap **2** is provided with longitudinal ribs **23** which indent the soft aluminum of which the cap **4** is typically fabricated, and help retain the cap **2**. The portions **41** and **43** of the cap **4**, if present, are of course broken away prior to application of the cap **2**.

The cap **4**, closure **60**, vial body **6** and piston **8** have already been described in detail above. The plunger **10** differs from that shown in FIGS. **1** and **2** in two respects. Its internal threads **20** end abruptly at abutments short of the front end of the plunger, so that when the plunger is screwed onto the extension of the piston, the abutments at the ends of the threads meet abutments at the ends of the external grooves on the extension which grooves in this embodiment stop short of the inner end of the extension, just before the inner end of the plunger contacts the rear surface of the piston. This prevents the plunger being screwed excessively tightly against the back of the piston in a manner which might result in rocking movements of the plunger being transmitted directly to the piston. Instead such movements are largely absorbed by the flexibility of the extension **18**. Secondly, the flange **26** at the rear end of the plunger is moulded so that about one half of its periphery is separated into an integral loop **11**, which can be flexed rearwardly about hinge lines **13**, and serves either as a thumb loop to assist manipulation of the syringe, or a suspension loop from which the syringe can be hung during infusion of its contents as discussed further below. The synthetic plastic material from which the plunger is moulded is selected from those having hinge forming capability such as many pharmaceutically acceptable grades of polypropylene.

In order to provide further stabilization of the plunger, to prevent its withdrawal from the body, and to provide a finger grip during manipulation of the syringe, particularly where longer vial bodies **6** are utilized, an optional plunger stabilizer and adapter ring **15** may be provided. This has axially extending inner flanges **150** which enter the inner end of the body, and retaining lugs **152**, which snap over the bead **7**. Openings **154** and flanges **156** may be provided on the rear surface of the ring, as required, to assist in adapting the syringe to infuser apparatus.

Where the contents of the vial are liquid and do not require reconstitution or dilution, or reconstitution is effected by a diluent or solvent introduced via a needle or cannula through the closure **60**, the cartridge cap **12** and diluent cartridge **14** are not required, the components already described constituting a complete syringe system. Otherwise these components may be provided and utilized as already described in relation to the embodiment of FIGS. **1** and **2**. The components themselves are however somewhat modified as shown in FIG. **4**, to facilitate handling. A skirt portion **120** of the cap is formed with longitudinal slots **122** extending from its rear edge, and inner lips **124** around the inner periphery of that edge, whilst a front extension of the cartridge **14** is provided with ribs **142** extending longitudinally between the peripheral ridges **36** and **38**, which ribs are accommodated by the slots **122**. The ribs **142** are continued beyond a peripheral groove behind the ridge **36**. The threads **30** and the cap **12** are reduced to short ridges between certain of the slots **122**. Because of the slots, the cap **12** is readily engaged over the ridge **38**, but when the assembly is inserted into the interior of the plunger **10**, the diameter of the cap relative to the internal chamber of the plunger **13** such that the lip **124** is pressed into the ring of shallow recesses defined between the ridges **36** and **38** and the ribs **142**, thus ensuring that the threads **30** may be engaged with the threads **20** within the plunger by turning the capsule, and inhibiting accidental forward movement of the cartridge **14** into the cap **12**.

The capsule **14** is blow moulded from a heat sealable, film grade, low melting, high ethylene random propylene-ethylene copolymer suitable for medical use. An example of such a material, already approved for pharmaceutical applications, is DYPRO (trade mark) polypropylene Z9350 from Fina Oil and Chemical Company which has a melting point

of about 130° C. Such a material, formed by injection of ethylene into a propylene matrix, combines necessary qualities of transparency, impermeability and flexibility with the stability to withstand sterilizing temperatures in an autoclave, despite its low melting point; the pressure in the autoclave is maintained at a sufficient level to prevent bursting of the capsule during sterilization. Conventional capsule materials are unsuitable for use in this application, since they lack at least one of the necessary properties of flexibility, transparency, impermeability, penetrability, compatibility with conventional pharmaceutical diluents, and ability to withstand sterilization temperatures without failure or degradation.

Utilization of syringes incorporating the above described modifications is similar to that already described. With a small modification to certain of the syringe components, the syringe contents may be reconstituted or diluted with fluid from an I.V. bag or minibag **160** and then injected into the bag for delivery, as shown in FIG. **6**. Both the inner and outer components of coupling adaptor **27** of the cap **2** are elongated, and the bores of the inner component of the coupling adaptor and of the needle **22** are sufficient to provide an air venting passage around the read end of the needle **22** when fitted to the adaptor **27**. A locking sleeve **29** on the needle **22**, which sleeve engages the adaptor **27**, is provided with a ventilation opening **31**, such that when the sleeve **29** is screwed partially onto the adaptor as shown, air can escape through the sleeve as fluid from the bag **160** enters the syringe through the needle **22**. When a desired amount of fluid has entered the syringe, the ventilation opening is closed by screwing the needle further onto the adaptor, following which the contents of the syringe may be injected into the bag **160**.

Referring to FIGS. **7–10** of the drawings, a syringe comprises a syringe barrel in the form of a somewhat elongated glass vial **202**, of which the bottom wall is absent apart from a slight inward projection of a strengthening bead **206** formed at the bottom of a side wall **204** of the vial and best seen in FIG. **20**. In the example shown the strengthening bead **206** also has a very slight outward projection, but this is far smaller than would be necessary if the bead were formed wholly externally of the side wall **204**, and may be entirely eliminated. In any event, the outward extent of the projection should be insufficient to prevent vials from standing very closely adjacent to one another without sufficient space to tip. Typically the projection will not exceed about one fifth of the total thickness of the bead. The projection of the bead on the inside should also be limited, both so that the head **210** of **1***a* moulded rubber piston **208** can be inserted into the vial past the projection (this is facilitated by the presence of peripheral grooves **212** in the head between sealing lands **214**), and so that a sleeve **218** of a combined finger grip, piston stop and plunger guide **216** (henceforth referred to as the finger grip) can be pushed past the projection whilst remaining a snug fit within the side wall of the vial. Insertion is facilitated by the slight flare provided at the bottom entry to the vial body by the rounding of the bead, and the insertion is readily mechanized.

The piston **208** is also provided with an integrally moulded downward extension **220** which is formed with a central cavity **223** to increase its flexibility relative to the head **210** of the piston which is substantially solid. The piston is dimensioned so that when it is inserted in the vial **202**, the lands **214** are compressed sufficiently to form a hermetic seal against the interior of wall **204** whilst permitting the piston to be moved longitudinally of the vial. Initially, the piston is located at the bottom of the vial (see FIG. **8**), with the bottom of extension **220** just within the vial so that it does not affect the ability of the vial to stand upright on its base formed by the bead **206**. The location of the fairly massive solid rubber piston **208** at the base of the vial helps stabilize the empty vial **202**, even when the height of the latter is somewhat greater relative to its diameter than is normally required for stability. The practical limit of the height to diameter ratio is set entirely by the requirement that the vials can be conveyed through a conventional vial filling and capping machine in a sufficient stable manner to permit reliable operation of the machine. In the example shown, the vial has an outside diameter of approximately 3 cm and a height of 12.8 cm for this diameter. A height of 14 centimeters is believed to approach the practical limit for stability, but this ratio will vary somewhat according to the relative wall thickness of the vial and the weight of the piston. Provided that the outward projection of the bead **206** is insufficient to affect stability, so that the vials can jostle without applying tipping force to each other, and assuming use of a piston generally as described, the maximum ratio attainable should be greater than 4, but will be less than 5.

The stopper **222** and cap **224** applied by the conventional vial filling and capping machinery may be of conventional construction, although the stopper **222** is preferably designed substantially to fill the neck of the vial so as to minimize dead space above the piston when the latter is pushed to the top of the vial (see FIG. **9**). This ensures that as much as possible of the contents of a syringe formed from the vial can be expelled by movement of the piston.

The cap **224** is preferably modified as shown in FIG. **9** and FIG. **10**. In FIG. **9**, a conventional main cap cooperates with a moulded plastic adaptor assembly comprising an annular flange **226** within the cap, a cylindrical extension **228** extending through the cap and a thin diaphragm **230** closing a bottom end of the extension. An internal thread **232**, similar to that provided on conventional syringe adaptors for receiving needles, such as those sold under the trade-mark LUER-LOK, is formed within the adaptor. A removable push on cap may be provided to close the open end of the adaptor during storage, being removed prior to use. In FIG. **10**, the cylindrical extension **228** is formed integrally with the aluminum cap, again with an internal thread **232**. I have found that the extension **228** can be accommodated by conventional vial capping machinery, at any rate with no more than minor modification, without interfering with the capping process, whilst the provision of such an extension enables the elimination of a separate adaptor cap, and the additional assembly step required to apply it.

In order to convert the vial into a syringe, either a double ended needle **234** of the blood collecting type may be applied directly to the extension **228** (see FIG. **10**) or an adaptor **236** (see FIGS. **7** and **9**) may be provided for any needle or alternative delivery device equipped with a standard syringe coupling so as to provide the latter with the capability of penetrating the stopper **222**, as well as the diaphragm **230** if present. The adaptor **236** has a needle **238** and external thread **240** at one end, the needle providing the penetration function and the thread **240** engaging the thread **232**, while its other end provides an internally threaded socket **242** and coaxial spigot **244** for forming a fluid-tight coupling to the needle or the like.

Prior to fitting the double ended needle **234**, or needle and adaptor **236**, a plunger **246** is applied to the extension **220** of the piston. The plunger has a shaft **248**, of cruciform cross-section in the example shown, an internally threaded sleeve **250** at its one end, and an end flange **252** at its other end. The sleeve **250** has internal multistart threads **254**,

complementary to external multistart threads **256** on the extension **220**. The lands between the threads **254** on the sleeve **250** and the threads **256** on the extension **220** both stop short respectively of the outer end of the sleeve **250** and the inner end of the extension **220** so as to form abutments **258**, **260** which prevent the sleeve **250** from being screwed tightly against the underside of the head **210** of the piston. This means that any tilting forces applied to the plunger are applied to the relatively flexible extension **220** and not directly to the head **210**, thus minimizing the risk of breaking the hermetic seal between the head **210** and the vial.

The plunger is formed of a hinge-forming synthetic plastic such as a pharmaceutical grade polypropylene, and a generally semicircular peripheral portion **262** of the flange and is separated from the remainder of a slot **264**, remaining connected only by thin, hinge-forming connections **266**. This portion **262** provides a finger loop which can be pulled rearwardly, as shown by broken lines in FIG. **1**, to facilitate handling of the plunger. As a supplemental or alternative feature, a notch **272** may be formed in the shaft **248** of the plunger, to provide a hook by means of which the syringe may be suspended when used in certain infusion applications.

In order to provide the various functions of preventing total withdrawal of the piston, forming a guide for the plunger and restricting its tilting movements, and providing a finger grip for the user, the combined finger grip and retainer **216** is pressed into the bottom of the vial **202** after filling and capping of the latter. It comprises the sleeve **218** and a peripheral flange forming oppositely extending finger grips **268**. It is also moulded from a pharmaceutical grade of plastic such as polypropylene. The sleeve **218** is a resilient press fit in the open end of the vial **204** so that it is slightly compressed by the internal projection of the bead **206** during insertion. Insertion of the retainer **216** may be facilitated by moderate warming of at least the retainer, and the slight flare provided by the rounding of the bead **206** also facilitates insertion. Beneath the grips **268** the sleeve has shallow arcuate grooves **270** in which the bead **206** snaps as the sleeve is pressed home. Forces applied to the grips **268** tending to pull the sleeve **218** away from the vial in turn tend to deform the sleeve, in such a manner as to increase the grip of the grooves **2700** on the bead thus resisting withdrawal of the sleeve.

During manufacture, the empty vials **204** are conveyed through a conventional sterilizing station, the piston **208** is inserted in each vial **204**, and the latter is filled and capped utilizing conventional vial filling and capping machinery (but preferably using a modified cap as shown in FIGS. **7** and **9** or FIG. **10**). The guide and finger grip **218** is then pressed into the base of the vial, which is shipped with the plunger **246** unattached. Prior to use, the plunger **246** is screwed onto the piston, and a needle or the like is applied to the extension **228**, utilizing an adaptor **236** if necessary so as to penetrate the stopper **222**, at which point the syringe is ready for use.

A modified configuration of the bottom end of the vial body is shown in FIG. **11**, in which an alternative approach is utilized to bringing the bead at the bottom end substantially within the diameter of the cylindrical vial body. Peripheral beads around the openings of glass bodies of this type are conventionally formed by flame softening the glass and adjusting the positioning and profile of the bead by rolling the body against suitable forming surfaces. In the FIG. **5** embodiment, a bottom portion **274** of the body **204** is flame softened and rolled so as slightly to reduce its diameter over about a length of typically 5–6 mm, and a fairly conventional out-turned rounded bead **206** is formed by flaring the bottom of this reduced diameter section. The reduction in diameter is such that at least the greater part of the bead is within the general diameter of the body. In the example shown, the outside diameter of the bead is very slightly greater than the general outside diameter of the body but this need not be so. In a typical example, the inside and outside diameters of the main portion of the vial body are 27 mm and 30 mm respectively, providing a wall thickness of 1.5 mm, and the reduction in diameter at the bottom is about 1 mm. The bead can then be formed by flaring the bottom end of the vial without increasing the outside diameter of the bead significantly beyond that of the main portion of the vial and typically by no more than 0.5 mm, even though a significant flare **276** can be provided and, because of the flare, the bottom contact line **278** of the vial when free-standing on a plane surface is substantially coincident with the outside diameter of the main body **204** of the vial, thus maximizing stability. Juxtaposition of the vial bodies in the event of jostling on a line will prevent any ramping tendencies which might otherwise occur with a flared bottom configuration of this type.

Whilst the presence of the piston after its insertion in the vial body acts to introduce a substantial mass which trends to stabilize the vial, the mass of the piston relative to that of the vial body will decrease as the height of the latter increases. Nevertheless it will result in a smaller rise of the centre of gravity of the assembly as the vial becomes higher than would otherwise be the case. It is also desirable that the vial bodies be stable without the piston present so that they may be conveyed through a stabilizer prior to insertion of the pistons. The present invention is particularly valuable in this respect since the disturbing influence of a bead at the open end projecting beyond the diameter of the main portion of the body is particularly severe under such conditions.

In order to cooperate with the modified vial body profile, the finger grip/retainer **216** must also be modified. The groove **270** is replaced by a bead **280** at the upper end of the cylindrical portion **218**, which bead may be moulded with a taper and if necessary with slots **282** to facilitate insertion, and/or the component **16** may be warmed to facilitate insertion. The bead must retain the component with sufficient tenacity to withstand pressures from the piston which may be developed through pressure build-up in the vial during normal storage, although it should be noted that pressure of the piston on the bead may actually help retain it by forcing it against the shoulder **284**. Alternatively or additionally, claws **286** may be moulded onto the component **216** to retain it by external engagement with the bead **206**.

A further development of the embodiment of FIG. **11** is shown in FIGS. **12** and **13**. A body **402** for a bottomless vial is moulded from glass or synthetic plastic material, with a generally cylindrical form having shoulders **404**, at the top end connecting to a hollow neck **406**. At a bottom end of the body its side wall is formed with a rounded or beaded bottom edge **408** to form an open bottom end through which a piston **410** may be inserted.

A portion **416** of the inside side wall adjacent the bottom edge **408** is tapered inwardly and joined to the remainder of the side wall by a peripheral jog **412** so as to provide a narrow internal upwardly facing annular shelf or shoulder **414** above a funnel-shaped upwardly tapered bottom entry to the interior of the body. The shelf and tapered bottom entry may be formed by rolling a heat softened bottom portion of the wall against a suitably shaped mandrel, in which case the outer face of the wall will be recessed as shown at **418**, or may be moulded in which case the outer recess may not be

present. In either case, there will be no projection, or at least no significant projection, of the outer face of the moulded or rolled portion of the wall outside the circumference of the remainder of the wall. The tapered bottom entry assists in insertion of the piston **410**, and subsequent insertion of the retainer ring **420** described below.

The retainer ring **420** is moulded from synthetic plastic material and provided with a radially extending flange **422**, and has a tapered upper portion **424** having a maximum diameter approximately equal to the internal diameter of the body **402** above the shelf **414**, but greater than the internal diameter of the shelf, and a minimum diameter such that it can readily start to enter the tapered bottom entry to the body. A lower portion **426** of the ring above the flange **422** has a smaller external diameter and a height at least equal to the height of portion **416** so that the ring may be pressed into the tapered entry until a shoulder **428** between the upper and lower potions snaps over the shelf **414**, thus positively retaining the ring. Preferably the lower portion **426** has an internal profile and height such as to provide snug accommodation of the portion **416** with due allowance for manufacturing tolerances. A small recess **430** may be formed in the inside wall of the body adjacent the shelf **414** to provide additional clearance for the shoulder **428**.

The flange **422** is of limited radial extent so that it does not extend beyond the external diameter of the vial body, so that the retainer ring **420** may be inserted prior to filling and capping, but in this case it cannot also provide a finger flange. This problem can be overcome if a flange is required by providing a separately moulded flange **432**, with an annular forwardly projecting locking ring **434** which can be snapped into annular groove **436** formed within the ring **420** prior to use of the vial.

I claim:

1. A pharmaceutical vial used for forming a barrel and a piston of a syringe after being filled and capped, comprising a cylindrical glass vial body having at one end an integral open neck and a peripheral external flange around an outer end of the neck, a peripheral rounded edge defining an inner periphery of an open opposite end, and a piston of resilient material having a cylindrical head within and concentric with the cylindrical glass body, the piston maintaining a slidable hermetically sealing relationship with a main inner cylindrical surface of the body, and being located to define a chamber of volume equal to the nominal capacity of the vial between the piston head and the neck of the vial, the piston having integral coupling structure wholly within the body for subsequent connection to a syringe plunger, and the vial being stable when standing on the open end of the body such that it can be conveyed while so standing through vial filling and capping machinery without tipping over, the body being formed adjacent said open end with peripheral radially extending positive retention means for engagement with complementary configurations of a tubular piston retaining member subsequently inserted within said open end of the body to resist overpressure within the body, wherein the retention means is formed by shaping a lower end portion of the body to have a reduced internal diameter such that the retention means is formed by an upwardly facing shoulder at the top of the lower end portion which projects inwardly of the projected circumference of said main interior cylindrical surface, and the lower end portion is located essentially within the projected circumference of a main cylindrical external surface of the body such as to leave the external surface of the body free of projections having an adverse effect on the stability of the vial;

said vial further including a pharmaceutically project within the chamber, a needle penetrable stopper inserted in the neck, and an annular cap crimped over said stopper and the flange of the neck to retain the stopper in hermetic engagement with the neck, the cap being provided with a concentric tubular outward extension for receiving one of a double ended hollow needle and an adaptor for receiving a single ended hollow needle such that one end of the double ended needle, or a hollow needle provided on the adaptor, can penetrate the stopper, and including a finger grip and piston retainer member, wherein the piston retainer member includes a tubular member which is a press fit within the open end of the body of the vial, and a flange at an outer end of the tubular member providing outwardly extending finger tabs, the tubular member being recessed in its external surface adjacent the flange in the vicinity of the finger tabs so as to receive the retention means inward of the interior wall of the body.

2. A vial according to claim **1**, wherein a generally cylindrical bottom portion of the body is of reduced internal and external diameter such as to provide a peripheral shoulder between said main internal cylindrical surface and an internal cylindrical surface of said bottom portion, and an outer cylindrical surface of said bottom portion has an external periphery which is essentially within the projected circumference of a main cylindrical external surface of the body, said shoulder forming said retention means, and the reduced internal diameter of the bottom portion being insufficient to prevent insertion of the piston therethrough.

3. A bottomless pharmaceutical vial for incorporation into a syringe, comprising a generally upright cylindrical hollow body with a narrower neck at its top end, a side wall of the body being formed with a bottom edge surrounding a flared bottom opening, with an inner surface of a lower portion of the side wall of the body adjacent said bottom opening extending upwardly to an outward jog in said inner surface, the jog forming an upwardly facing annular shoulder, and the lower portion of the side wall being substantially wholly within a downward projection of an outer surface of the remainder of the side wall, a piston within the body, and a piston retainer ring inserted into the bottom opening of the body beneath the piston, the piston retainer ring having an outer surface with an upper portion tapered to enter the flare of the inner wall of the body adjacent said bottom opening, a lower portion of reduced external diameter, and a downwardly facing shoulder connecting said upper and lower outer face portions, such that the ring may be pressed into said bottom opening until the shoulder snaps over the shelf to retain the ring.

4. A vial according to claim **3**, wherein the retainer ring is wholly inward of the downward projection of the outer surface of the side wall.

5. A vial according to claim **4**, wherein the retainer ring includes a flange extending beneath the bottom edge of the body but having a diameter no greater than that of the body.

6. A vial according to claim **5**, wherein the flange has an internal peripheral groove, and including a separately formed finger flange with a locking ring for subsequent engagement with the groove.

7. A vial according to claim **4**, including a separately formed finger flange for connection to the retainer ring following filling and capping of the vial.

8. Syringe kit, comprising:

(i) a first subassembly comprising:

(a) a glass pharmaceutical vial having an external configuration which is that of a glass serum vial and handleable by filling and caping machinery designed

for filling and capping serum vials, but with a circular bottom opening in a horizontal plane defined by a bottom edge if a cylindrical side wall of the vial, any external projection at said bottom edge of the said wall being insufficient to prejudice the stability of the vial when conveyed free-standing through such filling and capping machinery;

(b) a piston including means for subsequent coupling of said piston to a plunger, the piston being formed of resilient material and having sufficient solidity in the absence of the plunger to ensure an hermetic seal with said vial side wall, the piston, including said coupling means, being received wholly within said vial;

(c) a pharmaceutical filled within said vial above said piston through an open neck thereof by a vial filling machine; and

(d) a closure applied to the open neck at the top of the vial and retained thereon by an annular cap, the cap and closure being applied by vial capping machinery;

(ii) means applicable to said annular cap and axially displaceable on use of the syringe to project a cannula through said closure into said vial and thus place said vial in communication with means for injecting its contents;

(iii) a plunger engageable with said coupling means to enable the piston to be projected towards said neck within said side wall to expel said pharmaceutical through said injection means; and

wherein a shoulder is formed within said bottom edge of the cylindrical side wall, and further including a piston retainer ring engageable with the shoulder within the vial.

9. A kit according to claim **8**, further including means for providing a finger grip on said first subassembly and engaging said vial to facilitate operation of said plunger.

10. A kit according to claim **8**, wherein the axially displaceable means applicable to the annular cap and the plunger form parts of a second subassembly including said annular cap and the plunger.

11. In a method of producing a prefilled syringe for administering a pharmaceutical preparation, said syringe comprising a generally cylindrical syringe body having a neck at one end and a side wall having a bead finish at the other end, at least a component of the preparation filled into said body, an elastomeric closure closing the body at the neck end and secured by a cap, and an elastomeric piston at said other end forming a hermetic seal with an inside surface of said side wall, needle means for movement relative to the cap to penetrate the elastomeric closure, and plunger means for connection to an outer side of the piston, the improvement wherein:

the syringe is produced by associating components, including said plunger and said needle, with a prefilled vial produced by:

forming said body with height to diameter ratio such that the body is stable, and so that any outward extent of the bead is insufficient to result in interference such as would cause tipping, when the body is conveyed standing on said other end through equipment for filling and capping pharmaceutical vials;

inserting said elastomeric piston wholly within said other end of the body to form a vial open at the neck; and

filling said vial through said neck with said pharmaceutical preparation component, and then applying said elastomeric closure on said cap, whilst conveying the vial standing on said other end through equipment for filling and capping pharmaceutical vials.

12. A method according to claim **11**, wherein the association of other components includes engaging a piston retainer within said other end of the vial after filling and capping, and wherein the vial with the piston retainer applied is heat sterilized.

13. A method according to claim **11**, wherein the step of forming said body so that any outward extent of the bead is insufficient to result in interference such as would cause tipping includes forming the bead to provide an upwardly facing shoulder projecting inwardly of the wall of the body.

14. A method according to claim **11**, wherein the step of forming said body so that any outward extent of the bead is insufficient to result in interference such as would cause tipping includes slightly reducing the diameter of a bottom portion of the body, and flaring the open end of said reduced diameter portion of the body to form said bead.

* * * * *

EXHIBIT 17

US005137511A

United States Patent [19]

Reynolds

[11] Patent Number: 5,137,511

[45] Date of Patent: Aug. 11, 1992

[54] **SYRINGE**

[75] Inventor: David L. Reynolds, Montreal, Canada

[73] Assignee: Duoject Medical Systems Inc., Lac Brome, Canada

[21] Appl. No.: 437,203

[22] Filed: Nov. 16, 1989

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 72,015, Jul. 8, 1987, Pat. No. 4,886,495.

[51] Int. Cl.[5] A61M 5/00

[52] U.S. Cl. 604/88; 604/416; 604/413; 604/191

[58] Field of Search 604/82, 87, 88, 89, 604/91, 92, 191, 200, 201, 413, 414, 416

[56] **References Cited**

U.S. PATENT DOCUMENTS

2,542,814	2/1951	Hoskins	604/234
2,684,068	7/1954	Orens .	
2,728,341	12/1955	Roehr .	
2,828,743	4/1958	Ashkenaz et al. .	
2,832,340	4/1958	Dann et al.	604/228
2,842,126	7/1958	Brown .	
2,842,128	7/1958	Hein, Jr.	604/227
2,895,474	7/1959	Reznek	604/228
3,128,765	4/1964	Tint	604/228

(List continued on next page.)

FOREIGN PATENT DOCUMENTS

1766151	6/1971	Fed. Rep. of Germany .
632166	9/1982	Switzerland .
724671	2/1955	United Kingdom .
1030861	5/1966	United Kingdom .
1122787	8/1968	United Kingdom .
1252306	11/1971	United Kingdom .
1444119	7/1976	United Kingdom .
1496292	12/1977	United Kingdom .
1525455	9/1978	United Kingdom .

OTHER PUBLICATIONS

'Duocell Disposable Glass Syringe', International Medication Systems Limited (date unknown).

Catalog Page Showing 'Urojet', 'Puls-A-Jet' and 'Mini-Mix' Systems (date unknown).

'Vetter Lyo-Jet' Brochure, Vetter 1985.

"The Syringe-Phial 'Speed'", Steri Medical Supplies S.R.L. (date unknown).

'Kimble Glass Capabilities' brochure (date unknown).

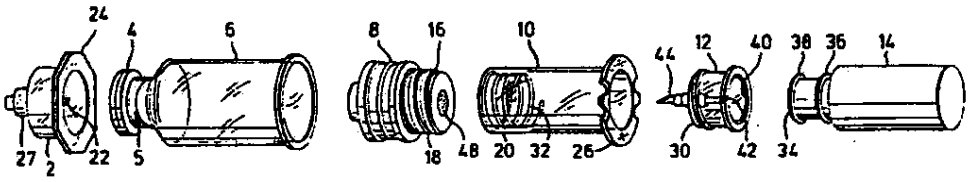
'West Capabilities . . . Glass Products' brochure (date unknown).

Primary Examiner—Stephen C. Pellegrino
Assistant Examiner—Ralph A. Lewis

[57] **ABSTRACT**

A prefilled syringe for one or two component medicaments is based upon the use of a vial containing a medicament or one component of a medicament, the vial having an open bottom closed by a piston. When a flexible extension of the piston is coupled with a tubular plunger, and an adaptor cap having an internal needle and an external connection for a needle is placed over a cap of the vial, the latter is converted into a prefilled syringe. The piston may have an axial passage closed by a resealable septum, so that a separate diluent stored in a flexible capsule may be introduced into the vial through the piston by a double ended needle mounted on a further cap applied to the capsule, the further cap being coupled within the tubular interior of the plunger so that the double ended needle penetrates the septum in the piston. The capsule is pushed forward onto the double ended needle when its contents are to be expelled into the vial. The capsule and its cap are then removed and discarded. In an alternative arrangement, the cap of the capsule is coupled to the adaptor cap and the diluent introduced into the vial through a closure secured by the cap of the vial, after which the capsule is removed from the plunger and the latter is coupled to the piston.

11 Claims, 8 Drawing Sheets



U.S. PATENT DOCUMENTS

3,150,661	9/1964	Maki .	
3,437,090	4/1969	Sarnoff .	
3,489,147	1/1970	Shaw .	
3,542,240	11/1970	Solowey .	
3,547,122	12/1970	Rinser .	
3,563,373	2/1971	Paulson .	
3,570,486	3/1971	Engelsher .	
3,636,950	1/1972	Gomez et al. .	
3,678,931	7/1972	Cohen .	
3,682,174	8/1972	Cohen .	
3,724,460	4/1973	Gomez et al. .	
3,785,379	1/1974	Cohen .	
3,845,763	11/1974	Cloyd .	
3,872,867	3/1975	Killinger .	
3,903,886	9/1975	Omotani .	
3,923,059	12/1975	Ogle .	
3,994,296	11/1976	Cloyd .	
4,014,330	3/1977	Genese .	
4,055,177	10/1977	Cohen .	
4,059,109	11/1977	Tischlinger .	
4,060,082	11/1977	Lindberg et al. .	
4,112,945	9/1978	Helixon et al.	604/232
4,171,698	10/1979	Genese .	
4,180,070	12/1979	Genese .	
4,390,016	6/1983	Riess .	
4,568,336	2/1986	Cooper .	
4,581,016	4/1986	Gettig .	
4,583,971	4/1986	Bocquet et al.	604/414
4,675,020	6/1987	McPhee	604/414
4,723,956	2/1988	Schnell et al.	604/408
4,731,068	3/1988	Hesse .	
4,755,169	7/1988	Sarnoff et al. .	
4,861,335	8/1989	Reynolds	604/191
4,886,495	12/1989	Reynolds .	
4,931,043	6/1990	Ray et al.	604/228

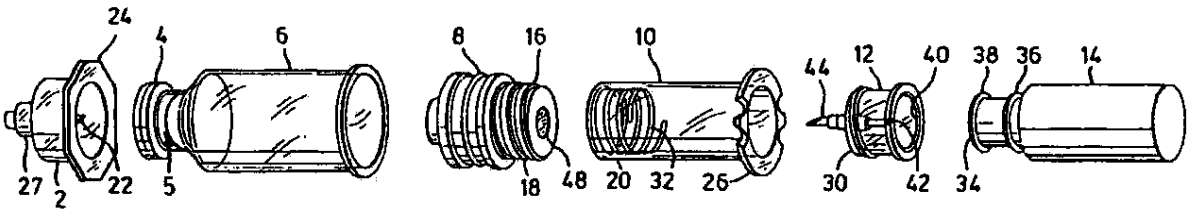

24
4
6
8
16
10
44
12
40
38
36
14
27
2
22
5
18
48
20
32
26
30
42
34

FIG. 1

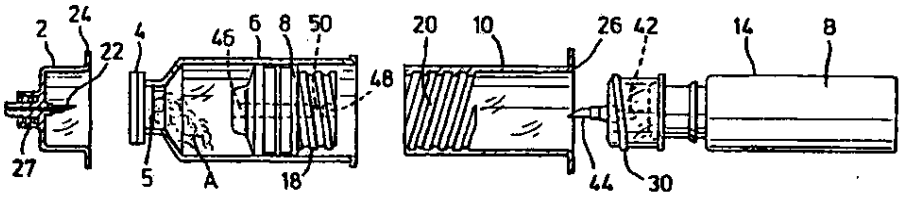

2
24
22
4
46
6
8
50
48
20
10
26
42
14
8
27
5
A
18
44
30

FIG. 2

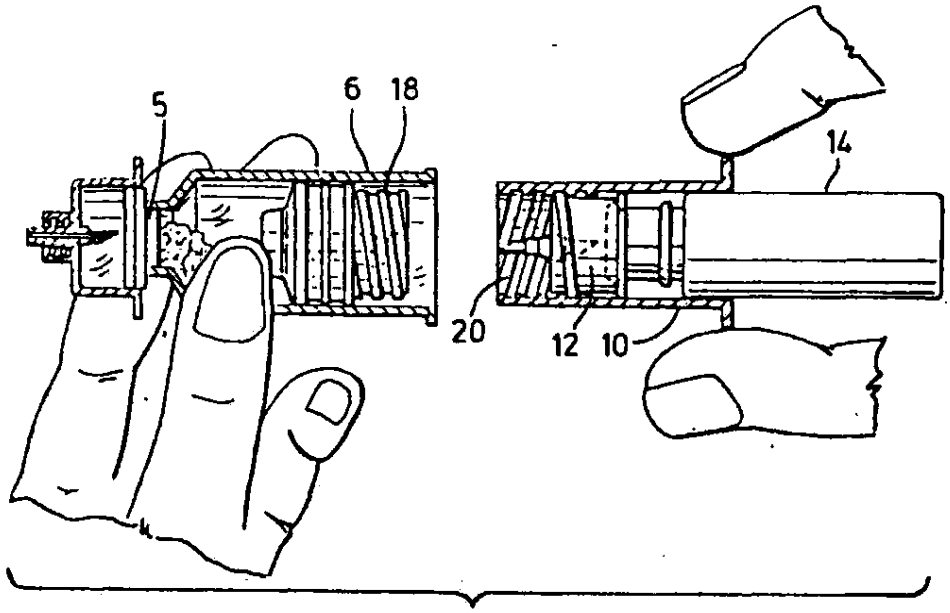


FIG. 3

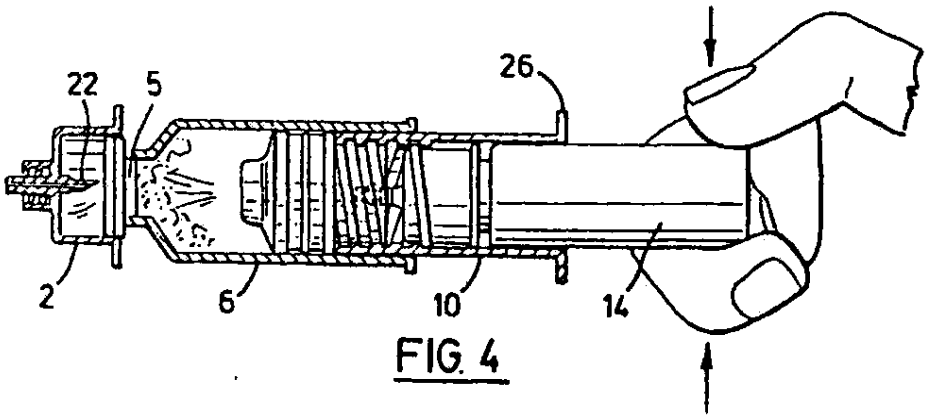


FIG. 4

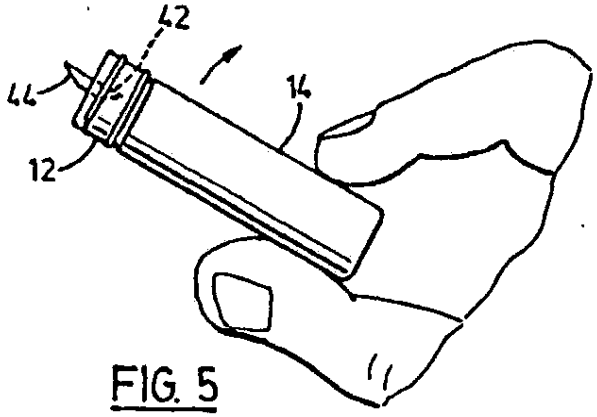


FIG. 5

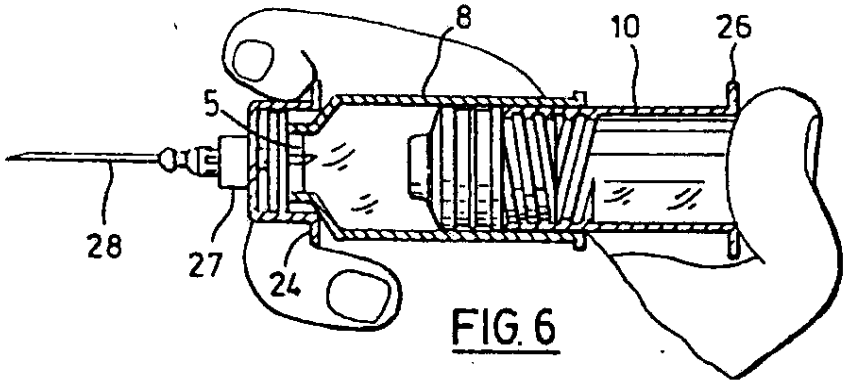


FIG. 6

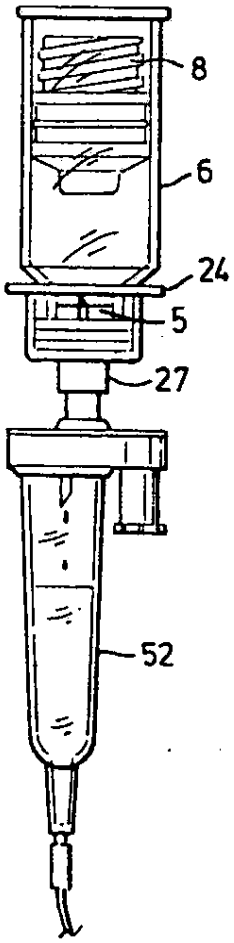


FIG. 7

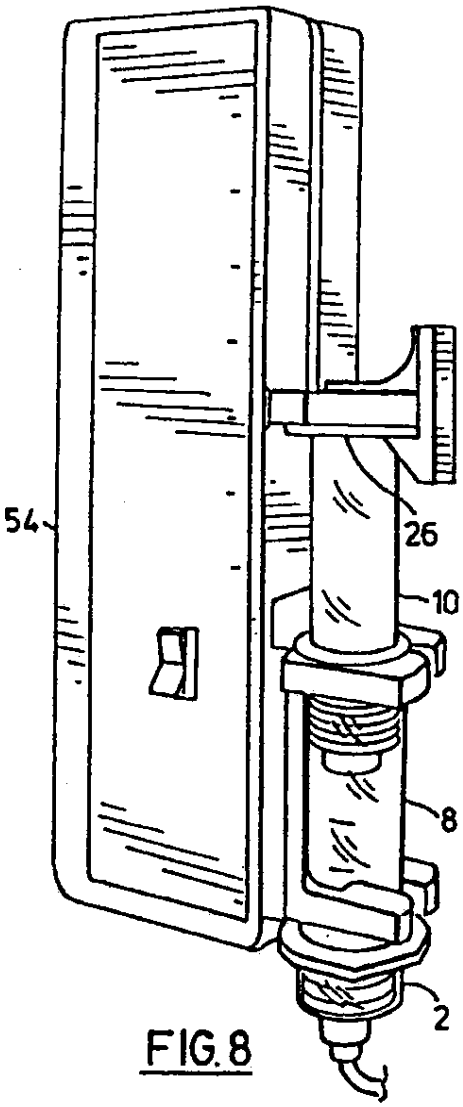
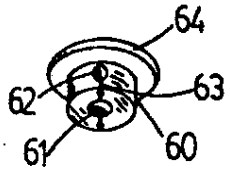


FIG. 8

FIG. 9



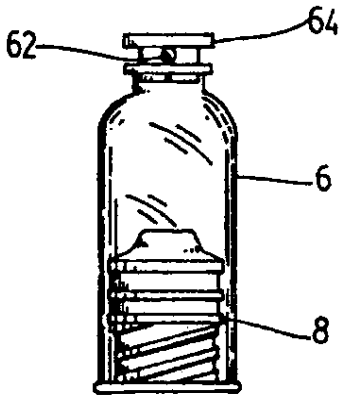


FIG. 10

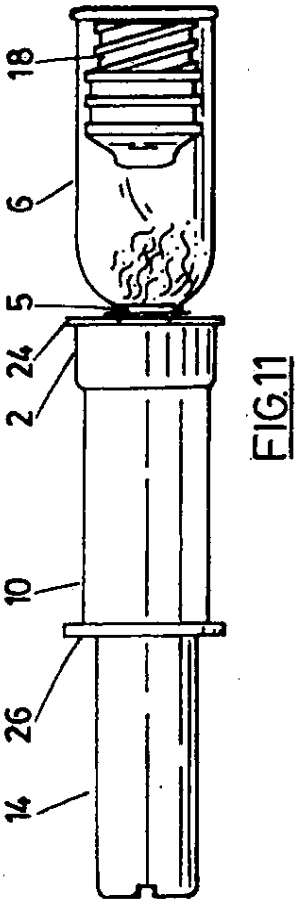


FIG.11

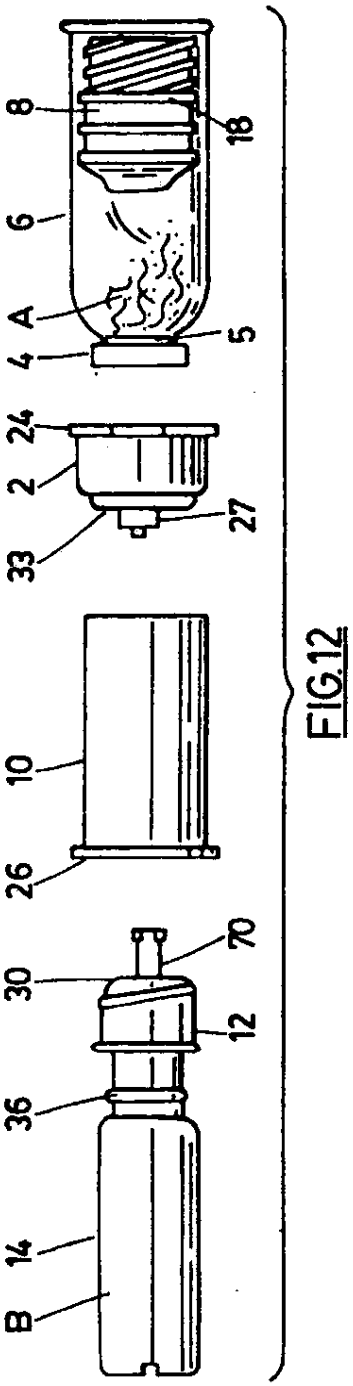


FIG.12

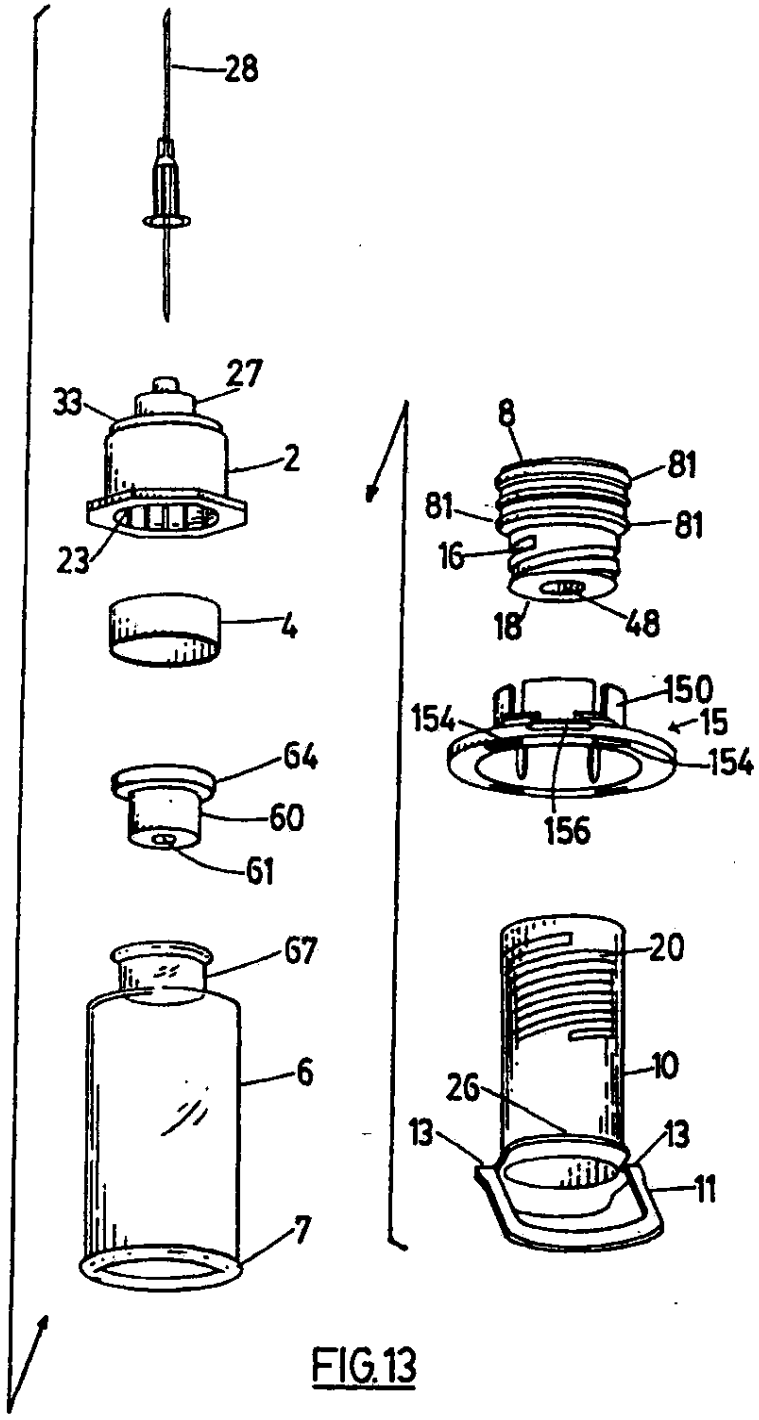

28
27
33
2
23
4
64
60
61
67
6
7
8
81
81
81
16
18
48
150
15
154
154
156
20
10
26
13
13
11

FIG.13

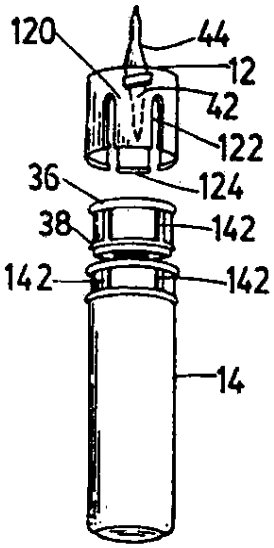

120
44
12
42
122
124
36
38
142
142
142
14

FIG. 14

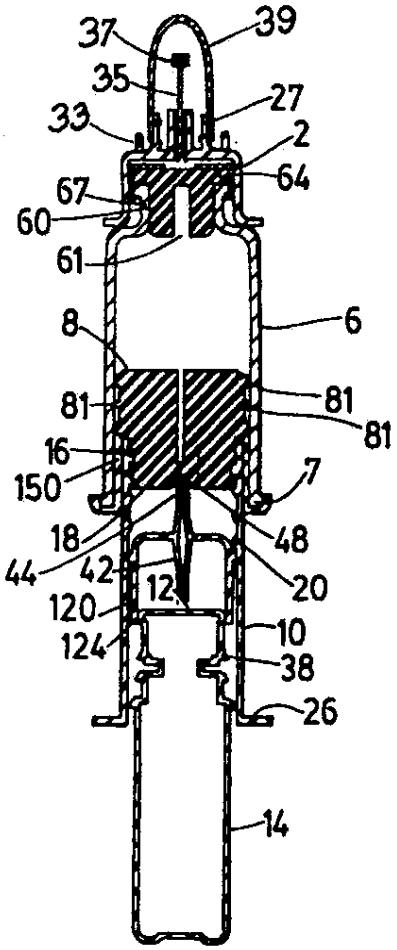

37
39
35
27
33
2
64
67
60
61
8
6
81
81
81
16
150
7
18
48
44
42
12
20
120
10
124
38
26
14

FIG. 15

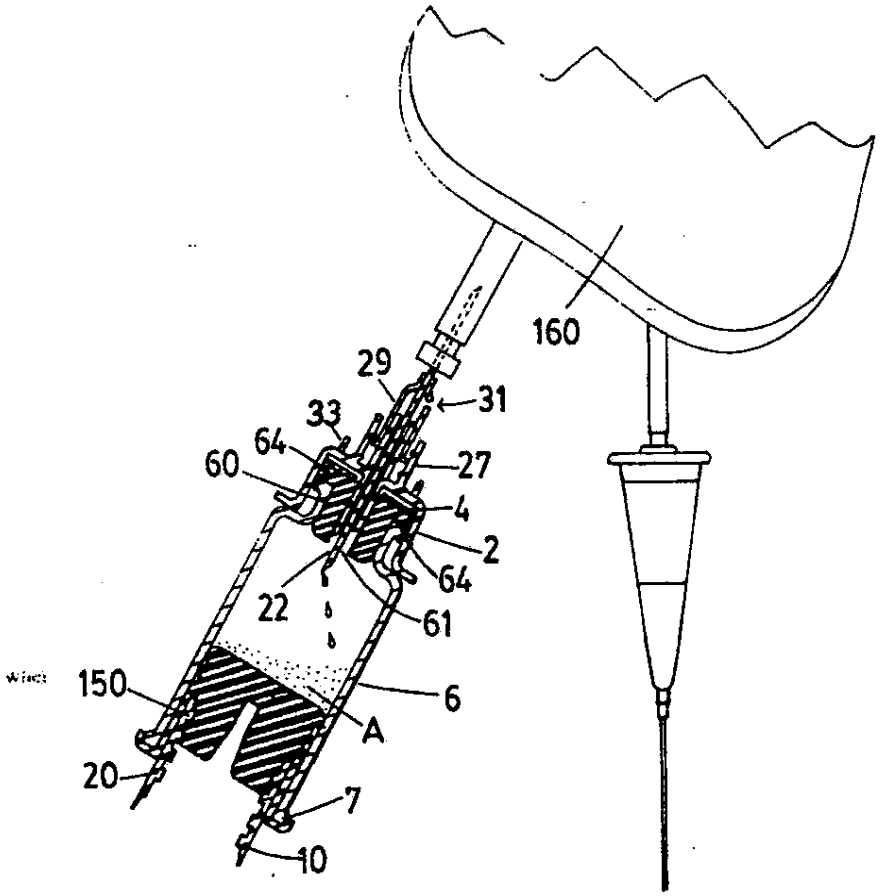


FIG. 16

SYRINGE

BACKGROUND OF THE INVENTION

This application is a continuation in part of Ser. No. 072,015 filed Jul. 8, 1987 now U.S. Pat. No. 4,886,495.

FIELD OF THE INVENTION

This invention relates to prefilled syringes for use in medical or veterinary treatment.

REVIEW OF THE ART

There has been an increasing trend in recent years to the putting up of pharmaceuticals in dosage forms so as to minimize the preparation required to administer a medicament to a patient and to reduce the chances of dosage errors or contamination. One dosage form which has been gaining rapid acceptance is the prefilled disposable syringe. Various difficulties are however associated with the preparation and usage of such syringes, particularly in the case of preparations which, in ready to use condition, have a short shelf life. Numerous forms of dual compartment syringe structures have been proposed for the shipping of such preparations with components stored in separate compartments for admixture immediately prior to use. Although certain structures have met with some degree of acceptance, they are commonly difficult to manufacture and/or use because of difficulties in filling the syringe with the components, and because they require extensive manipulation immediately prior to use. Moreover they are frequently substantially more bulky than conventional syringes because in many cases they frequently comprise components which effectively represent two syringes in tandem.

Problems in the manufacture of prefilled syringes are not confined to two component systems and even with single component systems the filling of syringes under factory conditions is difficult to mechanize effectively and requires expensive special purpose syringe filling machinery. The same applies to related units prefilled with liquids required for injection or infusion during medical procedures.

Another approach where single component systems are involved is exemplified by British Patent Specifications Nos. 1,252,306 and 1,444,119, and U.S. Pat. No. 4,445,895, in which a prefilled cartridge having a displaceable plug at one end, and a needle penetrable closure at an opposite end, is inserted into the barrel of a syringe for dispensing of its contents. Whilst such cartridges and the equipment for filling them are known and available, they are only really suitable for preparations which can be stored in liquid form, and require either a special or a modified syringe for their use. The cartridges themselves require special filling apparatus.

In a further arrangement disclosed in U.S. Pat. No. 3,845,763, a cartridge or vial is closed at its bottom end by a slidable plug with a downwardly extending stem, which cartridge or vial is inserted bottom end first into a special holder which carries a double ended needle, so that the stem is penetrated by the needle and the body of the vial is converted into a plunger which can be depressed to expel the contents of the vial through the stem. The projecting stem means that the vial cannot be filled utilizing conventional vial filling machinery.

The high capital expenditure involved in implementing known prefilled syringe systems has severely limited their adoption to those few cases where their advantages outweigh the substantial additional unit costs involved as compared to conventional modes of delivery.

SUMMARY OF THE INVENTION

The present invention seeks to provide a system for the distribution of preparations required for injection or infusion in liquid dosage form during medical procedures, which has a wide range of utility both for single component liquid preparations or for two component systems of which one component may be a solid, which utilizes a small number of components all suitable for mass production using material already approved for usage in such applications, and which is simple to assemble and can be filled utilizing equipment already available to most pharmaceutical manufacturers.

The system is based upon and built around a basic component in the form of a 'bottomless vial'. Such a bottomless vial has all of the characteristics of a conventional pharmaceutical vial, except that the glass base of the vial is replaced by a piston wholly received within the vial and designed to form a hermetic seal with its cylindrical side wall, the seal being maintained both when coupled and when uncoupled from a plunger releasably connectable to the piston for moving the latter axially of the vial. A particularly important characteristic of such a bottomless vial is that it can be conveyed, filled and capped reliably by conventional vial filling and handling equipment such as is already possessed by most pharmaceutical manufacturers. To this end, the bottomless vial must be free of features which would significantly compromise its stability when handled by such equipment. Thus any flange around the base of the vial must result in no more than a slight increase in the overall diameter of the vial, so as to avoid any substantial increase in its tendency to tip when jostled by other similar vials, and the center of gravity of the vial must not be displaced so far upwardly as to substantially reduce the stability of the vial.

The piston must be capable of maintaining a hermetic seal with the wall of the vial of integrity comparable to that achieved during capping of a conventional vial, and this seal should be maintained during manipulation of a syringe system incorporating the vial, during which the piston may be subject to non-axial forces transmitted to it by a plunger and tending to break the seal.

In the context of the invention, it should be understood that "vial" refers to a particular type of container, having a rather squat cylindrical body whose height compared to the diameter of its base is such that it may stand stably on its base whilst being conveyed through a vial filling machine and subsequently sealed and capped. Its body should also be free of external projections large enough to interact with other vials or the filling machinery in a manner such as to promote tipping. A vial has a neck with a large enough internal diameter to permit filling from a vial filling machine: solid filling materials will normally require a larger neck than liquids. Vials should not be confused with cartridges, which are comparatively long and slim, and cannot usually be filled utilizing vial filling machinery since they are too tall to rest in a stable manner on their bases.

Accordingly the present invention provides a vial formed of rigid transparent material and consisting of a cylindrical body, said body having an open bottom end

having an external diameter at most only slightly greater than that of the remainder of the body, but sufficient relative to the height and center of gravity of the vial as a whole to support the latter in a stable manner when conveyed standing on its open end through vial filling and capping machinery, injectable material within the body, a comparatively wide neck at the top of the body through which said injectable material is filled into the body, an external peripheral flange surrounding the neck, an elastomeric closure applied to the neck, a cylindrical cap clamped onto the flange of the neck and having an annular inward extending flange at a top end overlaying the closure to secure the closure to the neck with the closure presenting a needle penetrable central portion, an impervious substantially solid piston of resilient material sealingly received within said body at its lower end beneath said injectable material and above said open bottom end, and an extension integral with said piston, projecting downwardly from said piston but wholly within the body, for establishing a flexible connection to a syringe plunger in a zone between the piston and said open end of the body, whereby said vial may be converted into a syringe for ejection of the injectable material on movement of the piston towards the neck, by connection of said syringe plunger to said extension and connection of fluid conduit coupling means to said cylindrical cap.

The differences between such a vial and a conventional vial do not prevent it from being filled and capped in conventional vial filling and capping machinery; indeed, apart from the replacement of the bottom wall of the vial by a piston as specified, it is a conventional vial, and can be handled normally by the machinery during filling with either liquid or solid material. The presence of the piston which is relatively massive, in the lower part of the vial even helps stabilize the latter during filling. Furthermore, liquid filled vials may be lyophilized utilizing special stoppers either as known in the art or as described below. Obviously the cubic capacity of such a vial is less than the capacity of a conventional vial of comparable overall dimensions but for most purposes this is immaterial.

A vial in accordance with the invention may be converted into a syringe by the addition of a plunger coupled to the piston and an outer cap which acts as a needle carrier. More specifically, the syringe includes as well as the vial a syringe plunger connected to the flexible extension from the piston, and an outer cap engaged over the cap of the vial, the outer cap having a hollow needle projecting axially within the cap and a coupling for engagement with injection means and communicating with said hollow needle, the outer cap being axially movable relative to said cap of the vial from a position in which the needle ends short of the cap of the vial to a position in which it penetrates the cap of the vial. The plunger is provided with radially extending flanges for sustaining actuating forces applied to the syringe through a flange grip provided on the outer cap or on a plunger guide or piston stabilizer ring applied to the open end of the vial.

In a syringe for a two component medicament, it is necessary to provide for packaging of the second component and its admixture with the first component in the vial prior to dispensing. The invention thus further extends to a capsule assembly comprising a generally cylindrical sealed capsule having walls formed of a flexible needle penetrable material of suitable properties, a generally cylindrical neck defined by said walls at one end of the capsule, said neck having axially spaced inner and outer peripheral ridges, and a generally cylindrical cap applied to said neck so that a detent within the cap engages the outer peripheral ridge on the neck, a hollow cannula being formed integral with and passing through said cap so that an inner penetrating end within the cap ends short of the neck of the capsule and an outer end formed either in the form of a needle or a fluid coupling which extends outwardly of the cap, the cap being displaceable relative to the capsule to a position in which the detent rides over the inner ridge and the inner end of the needle penetrates the neck of the capsule, the cap and capsule being of a diameter such that they can enter the tubular plunger to a position in which the outer end of the cannula, if of needle form penetrates the septum of the piston when the plunger is engaged with the latter. An alternative arrangement may be used where the outer end of the cannula is a coupling, in which case the latter is connected to the coupling on the outer cap of the syringe, with the plunger being used as a support for the capsule prior to being coupled to the piston.

Thus the injection system comprises a sequence of components of which various sub-sequences can be combined to form injection systems for preparations requiring shipping and storage as two separate components, certain sub-sequences themselves having utility respectively as injection systems for single component liquid preparations. "Injection" is utilized broadly to cover hypodermic, intramuscular and intravenous injection, gravity and mechanical infusion, and injection into other vessels utilized in medical treatment or testing. For the purposes of description, the "front" or "top" end of an injection system will be considered the end of the system from which a liquid preparation is so injected.

The arrangement including the capsule assembly has a number of advantages in the manufacture and use of prefilled syringes for two component systems; furthermore, without the third cap and the sealed capsule containing the second component the remaining components provide, according to a further feature of the invention, advantages in the manufacture and use of prefilled syringes for single component systems. The third cap and sealed capsule provide, according to yet a further feature of the invention, an advantageous subsystem for various applications in which a sealed sterile source of a liquid is required for injection, or dropwise introduction into other containers used in medical procedures. With prefilled syringes for two components systems, either the capsule or the capsule and the third cap, may be sold, or shipped separately. This enables different diluents or sizes of capsule to be selected, or a common set of diluent capsules to be utilized with syringe assemblies containing different first components, thus simplifying inventory control.

Further features of the invention will become apparent from the following description of a preferred embodiment thereof with reference to the accompanying drawings.

SHORT DESCRIPTION OF THE DRAWINGS

FIG. 1 is a perspective exploded view of the mechanical components of a syringe system including a vial in accordance with the invention;

FIG. 2 is a partially longitudinally sectioned, partially exploded view of the syringe components showing some further details of their construction;

FIGS. 3, 4 and 5 illustrate preparation of the syringe system to provide a syringe ready for use;

FIGS. 6, 7 and 8 illustrate exemplary applications of the syringe;

FIGS. 9 and 10 illustrate an optional feature of a vial in accordance with the invention;

FIGS. 11 and 12 are elevational and exploded views of an alternative embodiment of the syringe system;

FIG. 13 shows the separated parts a further embodiment of the syringe system;

FIG. 14 shows, separated, a diluent capsule and cap for use with the system of FIG. 13;

FIG. 15 is a longitudinal cross section through the assembled system of FIGS. 13 and 14; and

FIG. 16 is a fragmentary view of a syringe in accordance with the invention utilized in conjunction with an I.V. bag.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring to FIGS. 1 and 2, a syringe system for the injection of a liquid preparation stored as two components comprises seven primary mechanical components, apart from the components of the preparation, which latter are shown in FIG. 2 but not FIG. 1. The components of the preparation typically comprise a first component A which may be in any physical state suitable for storage in vial, and a second liquid component B, typically but not necessarily sterile water. The liquid component B is stored in a sealed capsule 14 of flexible material, manufactured using conventional techniques from a material, usually synthetic plastic, which is compatible with the contents of the capsule. The first component is stored in a cylindrical vial 6, typically of glass, and capped by an annular cap 4 which retains a conventional needle penetrable sealing member accessible through a central opening in the cap. By a vial is meant a cylindrical vessel which can assume a stable upright position supported by its base, the overall height of the vessel preferably not exceeding 2.5 times the external diameter of the rim of its base so that it remains stable when passing through conventional vial filling and capping equipment utilized to fill and cap the vial. A neck at the upper end of the vial 6, which is capped by the cap 4, has a relatively internal diameter characteristic of such vessels, usually not less than about 7.5 mm for liquid or 10 mm for solids, so that filling either liquids or solids can be readily achieved. The cap 4 is formed by an aluminum sleeve, having a flange retaining a sealing member formed by a soft rubber disc or plug 5 over or in the front end opening, and tightly crimped onto a neck at the front end of the vial so as to seal the latter. A major difference from conventional vials is that the conventional bottom wall of the vial is replaced by an axially movable piston 8 wholly within the vial and in sealing contact with the vial walls. When received within the vial 6, this piston in no way interferes with the handling of the vial using conventional machinery, and in particular permits the vial to be stood on its base with its neck (which forms the front end of the vial when in use) upwards as it passes through the filling and capping equipment.

The filled vial 6 may be converted into a prefilled syringe by applying an outer cap 2 over the cap 4 and positively attaching a cylindrical plunger sleeve 10 to the piston 8. The piston 8, typically formed of rubber, is moulded with a rearward extension 16 with an external thread 18, whilst the interior of the front end of the plunger sleeve 10 is formed with a complementary internal thread 20 so that it may be screwed onto the piston 8. The outer cap 2 fits over the inner cap 4 so that a hollow needle 22 formed within the cap 2 does not reach the penetrable zone of the cap 4. On the front of the cap 2 and in communication with the hollow needle 2 is a coupling adapter 27, for example similar to those sold under the trade mark LUER-LOK, for connection of the syringe to a needle 28 or other instrumentality (see FIGS. 6-8). To prepare the syringe for use, the outer cap 2 is pulled back over the inner cap 4 so that the needle 22 penetrates the cap, and the needle 28 or other instrumentality is applied. This should be done without pressing on the plunger sleeve so as to avoid accidental ejection of the contents of the syringe. The rear ends of both cap 2 and the sleeve 10 are formed with radially extending flanges 24 and 26 respectively which form finger grips for operation of the syringe. Thus if a user grips the syringe by the flanges as shown in FIG. 6 and presses them towards each other, the contents of the syringe can be expelled through the needle 22 and the needle 28. It will be noted that the rear end of the vial 6 is formed with only a relatively slight external bead 7 rather than the wide finger flange commonly found on the barrels of conventional syringes. In the present arrangement, the flange 24 provides the function of such a finger flange, enabling the bead 7 to be reduced to a size which will avoid such interference between the flanges of adjacent vials as would cause tipping when the vials are conveyed in a vertical attitude through filling and capping equipment.

In many applications, it is desirable to prevent premature penetration of the plug 5 by the needle 22, and therefore the cap 2 may be moulded with short internal threads (not shown) which prevent rearward movement of the cap 2 unless it is twisted so that the threads bite into the soft aluminum of the cap 4 and draw the cap 2 rearwardly so that the needle 22 can penetrate the plug.

A prefilled syringe constructed as discussed above has significant advantages over conventional prefilled syringes in that the vial may be filled using conventional vial filling equipment, and yet may be utilized directly instead of requiring its contents to be transferred to a syringe prior to use as has been conventional in the use of vials.

The vial may also be charged with material which is not directly injectable, such as solids which must be dissolved or suspended in a liquid medium prior to injection. In this case the liquid medium is sealed as already described in a flexible capsule 14. A third cap 12 is either applied to the capsule as shown in FIG. 2, or inserted into the plunger sleeve 10 so that a screw thread 30 on the exterior of the cap engages the screw thread 20 within the sleeve.

A neck 34 of the capsule 14 has two peripheral ridges 36 and 38. If the cap 12 is applied to the capsule, a detent 40 within the cap is pushed over only the outer ridge 38 so that a rear end portion 42 of a hollow needle mounted in the cap stops short of the end of the capsule. By forcing the detent 40 rearwardly over the ridge 36, the needle portion 42 can be forced rearwardly so as to penetrate the capsule. A forward end portion 44 of the hollow needle has a length such that when the cap 12 is screwed into the sleeve 10, and the sleeve 10 is screwed onto the piston 8, the needle portion 44 penetrates a resilient septum 50 normally separating axial passages 46 and 48 formed in the front and rear of the piston.

In use, if the capsule 14 and cap 12 are shipped as a separate unit, this unit is screwed into the sleeve 10 (see FIG. 3), and the sleeve 10 is pushed into the rear of the vial 6 so that the needle portion 44 penetrates the septum 50 of the piston 8 and the thread 20 is screwed onto the thread 18 of the piston (see FIG. 4). This action also substantially unscrews the cap 12 from the thread 20. The capsule 14 is then pressed forward onto the needle portion 42, and the liquid contents of the capsule can then be squeezed through the needle and into admixture with the first component in front of the piston 8. Thereafter the capsule 14 and cap 12 may be pulled as a unit from the sleeve 10 and discarded (see FIG. 5). The septum 50 reseals as the needle portion 44 is withdrawn, leaving a syringe ready for use as illustrated in FIGS. 6–8. Alternatively, if the cap 12 is prefitted to the sleeve, the sleeve 10 may be screwed onto the piston 8, and the capsule 14 pressed into the sleeve 10 and the cap 12 so as to establish communication between the capsule and the space forward of the piston, the procedure thereafter being the same.

Rather than being used conventionally with a needle as shown in FIG. 6, the prepared syringe may be used for gravitational or mechanical infusion as shown in FIGS. 7 and 8. In FIG. 7, the adapter 27 is fitted to a complementary coupling on a gravity infuser 52 to provide a drip feed, the sleeve 10 having been unscrewed and discarded, together with the cap 12 and capsule 14, if used. In FIG. 8, the syringe is mounted in a mechanical infuser 54 such as that sold under the trade mark BARD, the latter being equipped with clamps 56, 58, 60 suited for engagement with the syringe.

By basing the system on an open-bottomed vial 6 closed at its bottom end by a piston 8 equipped with means such as the screw thread 18 for coupling it to a plunger of sleeve form, and with a needle penetrable septum 50, in optional conjunction with sealed flexible capsules of diluent, great flexibility in application can be obtained, using components which are easy to fill, compact to ship, and easy to make ready for use.

Referring now to FIGS. 9 and 10, the rubber disk or plug retained by the cap 4 on the vial 6 may be replaced by a modified plug 60 as shown in perspective from beneath and one side in FIG. 8, and partially installed on a vial 6 in FIG. 9. Use of such a plug 60 is advantageous when the solid component of a medicament is to be prepared in situ in the vial by lyophilization. The vial is filled with a liquid preparation to be lyophilized, and plug 60 inserted to the position shown in FIG. 9, so that the interior of the vial communicates with its environment through a central passageway 61 and radial bores 62, the passageway and the bores being no larger than needed for the removal of water vapour during lyophilization. The plug is split at 63 to facilitate moulding. After filling the contents of the vial are rapidly frozen and vacuum dried to leave a solid residue in the vial which can be reconstituted immediately before use. The plug 60 is then moved to the full extent permitted by a flange 64 into the neck of the vial 6 and secured by a cap 4. Whilst a conventional lyophilization stopper could be utilized in place of the plug 60, the latter has the advantage of minimizing the amount of liquid trapped within the stopper during use of the syringe. For the same reason, the head of the piston 8 is shaped so as to minimize dead space in the neck of the vial when the contents of the vial are expelled during use of the syringe.

FIGS. 11 and 12 illustrate an alternate configuration of the syringe. The various components are essentially identical to those already described, and the same reference numerals are utilized except that the outer needle 44 of the conduit extending through the cap 12 is replaced by an extension 70 which is configured at its outer end to couple with a standard syringe coupling such as the coupling 27 on the cap 2. This enables the capsule 14, once inserted in the plunger 10, to be locked through the extension 70 and the coupling 27 to the cap 2 to produce the compact assembly shown in FIG. 11. The inner end of the plunger 10 is a press fit on an annular retaining flange 33 formed on the cap 2. To prepare the syringe for use, the cap 2 is forced rearwardly over the cap 4 so that the needle 22 (see FIG. 2) pierces the seal 5, and the capsule 14 is forced forward so that it is pierced by the needle 42 and its contents can be expelled through the needle 42, the extension 70, the coupling 27 and the needle 22 into the vial 6. The assembly of the capsule 14 and the plunger 10 can then be released from the remainder of the syringe by turning so as to release the extension 70 from the coupling 27, a needle (not shown) may be applied to the coupling 27, the capsule 14 is removed from the plunger 11 and discarded, and the plunger 11 is screwed onto the coupling 18 to ready the syringe for use. With this arrangement, the passage 46 in the piston 8 is not required, although the passage 48 may be retained to save material and enhance the flexibility of the extension 18 of the piston.

A similar arrangement may be utilized for single component medicaments in which case the capsule 14 and cap 12 are not provided. The arrangement is advantageous for both single and multiple component medicaments since only the vial need be assembled and filled in a clean room, the only additional step required over the filling of a conventional vial being the insertion of the piston 8. The plunger 10 may be pressed onto the cap 2, and this assembly, if desired together with a needle and/or a capsule 12 and cap 14, may be separately sterilized and packaged, without endangering the stability or destroying the contents of the vial, which will often be sensitive to heat or radiation utilized for sterilization purposes. Since the capsule 12 can withstand conventional terminal sterilization techniques (see further below), it can be sterilized independently of the vial. This is a major advantage over many two-component syringe systems in which the components are separated only by some form of penetrable plug or diaphragm and must therefore either be fully assembled in a clean room, or subjected in assembled form to terminal sterilization techniques which may destroy or damage a component of the pharmaceutical preparation.

Where the capsule 12 is not being used, it is possible to utilize a cap 2 in which the needle 22 is not provided, and instead use a needle arrangement as shown in FIG. 13 or FIG. 15.

Features of presently most preferred embodiments of the invention are shown in FIGS. 13–15. The same reference numerals are used to denote the same parts in these figures as in the previous embodiments, where applicable, and construction and operation are similar except where otherwise indicated.

FIG. 13–15 show a further vial and syringe system according to the invention, the vial comprising a body 6 of rigid transparent material, usually glass although synthetic plastic resins might be utilized in certain applications. The body has the general configuration of a conventional vial except for the absence of a bottom wall. In order to compensate for the strengthening ef-

fect which would be provided by the bottom wall, in order to provide a detent for an optional plunger stabilizer ring 15 described further below, and in order to permit a slight flare at the extreme bottom end of the vial, a rounded bead 7 is provided around the perimeter of the bottom end of the body, although its peripheral extent should not be sufficient to increase substantially the diameter of the vial or decrease substantially its stability during handling.

A medicament A is retained within the vial by a piston 8. A closure 60 substantially fills a neck portion 67 of the vial after the vial, closed at the bottom by the piston, has been filled through its neck portion by a conventional vial filling machine. Although the medicament shown in a solid, it may be a liquid, or filled as a liquid and lyophilized to leave a solid residue. The piston 8 is moulded from rubber, preferably of at least 50 durometer hardness, and is formed with multiple, preferable three, peripheral ribs 81 on its outer surface, the external diameter of the ribs being slightly greater than the internal diameter of the body 6 so that an hermetic seal is established when the piston is pressed into the bottom of the body, initial entry being assisted by the flare mentioned above. The piston is moulded as a substantially solid body so that it has sufficient rigidity to maintain the desired hermetic seal with the body, any central bores within the piston (see FIG. 15) required to assist needle penetration being of insufficient radial extent to have any significant effect on its rigidity. Although in the piston shown in FIG. 16, a central bore 48 does just extend into the piston proper, its axial extent within the piston and its diameter are sufficiently small relative to the piston diameter that the rigidity of the piston is not substantially reduced. The longer bore 46 through the piston shown in FIG. 15 is of even smaller diameter so as not to prejudice piston rigidity.

The piston has a downward extension 18 of reduced diameter, in which the bore 48 is also present. The diameter of the bore 48 forms in this case a greater portion of the diameter of the extension 18, whose flexibility is thus somewhat increased by its presence. The extension carries on its outer surface a multistart thread, defined by grooves 16 which terminate abruptly short of the piston, forming abutments serving a purpose discussed further below. Provided that the hardness and rigidity requirements for the piston as a whole are met, the rubber utilized to form the piston, and any external coating on the rubber (which may act to increase the effective hardness of the rubber), are selected for compatibility with the medicament contained in the syringe, a number of approved materials being available and well known in the pharmaceutical art.

The neck closure 60 may be formed of similar rubber, and is similar in construction to that shown in FIGS. 9 and 10 if lyophilization of the syringe contents is required: otherwise the slot 63 and bores 62 (see FIG. 9) may be omitted. After insertion of the closure 60, its flange 64 may be held in place by a conventional cap 4 crimped over the flange and a flange on the neck of the bottle. Such a cap 4 may have a flip-off top attached to a separable central portion of the cap, partially severed from the remainder of the cap so that these portions may be broken away prior to assembly of the syringe to expose a central needle penetrable zone of the closure 60 above the bore 61.

The piston together with its extension 18 is relatively massive, with a weight which typically amounts to at least a major portion of that of the body 6. This weight in the lower part of the body assists in stabilising the vial during handling and filling and further inhibits tipping.

As mentioned above, vial assembly and filling will normally be performed in a clean room, since many pharmaceuticals will not withstand terminal sterilization procedures. The only additional step which requires to be carried out in the clean room other than is conventional in the filling of vials is the insertion of the piston 8.

In order to convert the basic vial into a syringe system, either one of two different approaches can be used, similar respectively to those described with reference to FIGS. 1 to 6 and FIGS. 11 and 12 above. Only the differences from that corresponding to FIGS. 1 to 6 will be described in detail for the present embodiment, since the differences from the system of FIGS. 11 and 12 arrangement will in general be similar. FIGS. 13 and 14 show the components of a syringe system separated, whilst FIG. 15 shown them assembled and sectioned (although an alternative needle arrangement is shown in FIG. 15). It should be understood that the diluent cartridge 14 and cartridge cap 12 are optional features of the system and will only be utilized when a diluent or solvent is required for the content of the vial which is not provided by some other means. When building a system similar to that shown in FIGS. 11 and 12, the same parts will be used, except that if the cartridge 14 and the cap 12 are used, the cap 12 will be modified in the manner illustrated in FIGS. 11 and 12. Assembly in the manner described with reference to FIGS. 11 and 12 has the advantages already described.

Referring to FIGS. 13 and 15, an outer cap 2 is pushed over the cap 4, and is similar to that shown in FIGS. 1, 2 and 12, except that the internal needle 22 shown in FIGS. 1 and 2 is omitted, the syringe being utilized with an alternative needle arrangement. In FIG. 13, a conventional double ended needle 28, is shown, the inner end of which replaces the needle 22.

FIG. 15 shows an arrangement in which the needle 28 may be single ended, an auxiliary hollow needle 35 being provided with a cylindrical sleeve 37 at the top which replaces the outer extremity of the inner portion of the coupling 27. A cap 39 is provided to retain the needle 35 within the coupling 27 until the needle 28 is fitted. When the syringe is to be used, the cap 39 is removed, and the sleeve of the needle is placed over the sleeve 37 and pushed down so that the needle 35 can penetrate the top of the vial and the needle 28 can be engaged with the coupling 27.

These needle arrangements are preferred for a syringe which is shipped in an essentially ready-to-use form, since the cap 2 may be pushed fully onto the cap 4 during assembly, yet the closure 60 remains unpenetrated until the needle (or other instrumentality as discussed below) is fitted at the time of use. On the other hand, the integral needle 22 is convenient where the assembly is to be utilized in the manner shown in FIGS. 11 and 12 and a capsule 12 is utilized. The inner surface of the cap 2 is provided with longitudinal ribs 23 which indent the soft aluminum of which the cap 4 is typically fabricated, and help retain the cap 2. The portions 41 and 43 of the cap 4, if present, are of course broken away prior to application of the cap 2.

The cap 4, closure 60, vial body 6 and piston 8 have already been described in detail above. The plunger 10 differs from that shown in FIGS. 1 and 2 in two respects. Its internal threads 20 end abruptly at abutments short of the front end of the plunger, so that when the

plunger is screwed onto the extension of the piston, the ends of the threads meet adjustments at the abutments at the ends of the external grooves on the extension, which grooves in this embodiment stop short of the inner end of the extension, just before the inner end of the plunger contacts the rear surface of the piston. This prevents the plunger being screwed excessively tightly against the back of the piston in a manner which might result in rocking movements of the plunger being transmitted directly to the piston. Instead such movements are largely absorbed by the flexibility of the extension **18**. Secondly, the flange **26** at the rear end of the plunger is moulded so that about one half of its periphery is separated into an integral loop **11**, which can be flexed rearwardly about hinge lines **13**, and serves either as a thumb loop to assist manipulation of the syringe, or a suspension loop from which the syringe can be hung during infusion of its contents as discussed further below. The synthetic plastic material from which the plunger is moulded is selected from those having hinge forming capability such as many pharmaceutically acceptable grades of polypropylene.

In order to provide further stabilization of the plunger, to prevent its withdrawal from the body, and to provide a finger grip during manipulation of the syringe, particularly where longer vial bodies **6** are utilized, an optional plunger stabilizer and adapter ring **15** may be provided. This has axially extending inner flanges **150** which enter the inner end of the body, and retaining lugs **152**, which snap over the bead **7**. Openings **154** and flanges **156** may be provided on the rear surface of the ring, as required, to assist in adapting the syringe to infuser apparatus such as that shown in FIG. **8**.

Where the contents of the vial are liquid and do not require reconstitution or dilution, or reconstitution is effected by a diluent or solvent introduced via a needle or cannula through the closure **60**, the cartridge cap **12** and diluent cartridge **14** are not required, the components already described constituting a complete syringe system. Otherwise these components may be provided and utilized as already described in relation to the embodiments of FIGS. **1** to **6** or FIGS. **11** and **12**. The components themselves are however somewhat modified as shown in FIG. **14**, to facilitate handling. A skirt portion **120** of the cap is formed with longitudinal slots **122** extending from its rear edge, and inner lips **124** around the inner periphery of that edge, whilst a front extension of the cartridge **14** is provided with ribs **142** extending longitudinally between the peripheral ridges **36** and **38**, which ribs are accommodated by the slots **22**. The ribs **142** are continued beyond a peripheral groove behind the ridge **36**. The threads **30** and the cap **12** are reduced to short ridges between certain of the slots **122**. Because of the slots, the cap **12** is readily engaged over the ridge **38**, but when the assembly is inserted into the interior of the plunger **10**, the diameter of the cap relative to the internal chamber of the plunger **13** such that the lip **124** is pressed into the ring of shallow recesses defined between the ridges **36** and **38** and the ribs **142**, thus ensuring that the threads **30** may be engaged with the threads **20** within the plunger by turning the capsule, and inhibiting accidental forward movement of the cartridge **14** into the cap **12**. Further turning of the capsule drives the needle **44** forward into the bore **48** (see FIG. **14**) and thence through a septum in the bore into a small diameter counterbore **46** through the head of the piston (similar to that shown in FIG. **2**), a piston modified in this manner being utilized when a diluent cartridge is to be used. The cartridge can then be forced forward so that the lips **124** ride over the ridge **38**, permitting the needle **42** to penetrate the capsule whose contents can then be transferred to the vial by squeezing and/or aspiration.

Provided that the cap **12** is provided with a coupling **70**, the capsule can of course also be utilized as described with reference to FIGS. **11** and **12**, in which case the passage **46** in the piston is not required.

The capsule **14** is blow moulded from a heat sealable, film grade, low melting, high ethylene random propyleneethylene copolymer suitable for medical use. An example of such a material, already approved for pharmaceutical applications, is DYPRO (trade mark) polypropylene Z9350 from Fina Oil and Chemical Company which has a melting point of about 130° C. Such a material, formed by injection of ethylene into a propylene matrix, combines necessary qualities of transparency, impermeability and flexibility with the stability to withstand sterilizing temperatures in an autoclave, despite its low melting point; the pressure in the autoclave is maintained at a sufficient level to prevent bursting of the capsule during sterilization. Conventional capsule materials are unsuitable for use in this application, since they lack at least one of the necessary properties of flexibility, transparency, impermeability, penetrability, compatibility with conventional pharmaceutical diluents, and ability to withstand sterilization temperatures without failure or degradation.

Utilization of syringes incorporating the above described modifications is similar to that of the other embodiments already described. The contents of the syringe may be delivered as already described with reference to FIGS. **6**, **7** or **8**, or in other ways. With a small modification to certain of the syringe components, the syringe contents may be reconstituted or diluted with fluid from an I.V. bag or minibag **160** and then injected into the bag for delivery, as shown in FIG. **16**. Both the inner and outer components of coupling adaptor **27** of the cap **2** are elongated, and the bores of the inner component of the coupling adaptor and of the needle **22** are sufficient to provide an air venting passage around the read end of the needle **22** when fitted to the adaptor **27**. A locking sleeve **29** on the needle **22**, which sleeve engages the adaptor **27**, is provided with a ventilation opening **31**, such that when the sleeve **29** is screwed partially onto the adaptor as shown, air can escape through the sleeve as fluid from the bag **160** enters the syringe through the needle **22**. When a desired amount of fluid has entered the syringe, the ventilation opening is closed by screwing the needle further onto the adaptor, following which the contents of the syringe may be injected into the bag **160**.

The syringe of the invention is of course compatible with other syringe based drug administration systems.

I claim:

1. A vial formed of rigid transparent material and consisting of a cylindrical body, said body having an open bottom end having an external diameter at most only slightly greater than that of the remainder of the body, but sufficient relative to the height and center of gravity of the vial as a whole to support the latter in a stable manner when conveyed standing on its open end through vial filling and capping machinery, injectable material within the body, comparatively wide neck at the top of the body through which said injectable material is filled into the body, an external peripheral flange

surrounding the neck, an elastomeric closure applied to the neck, a cylindrical cap clamped onto the flange of the neck and having an annular inward extending flange at a top end overlapping the closure to secure the closure to the neck with the closure presenting a needle penetrable central portion, an impervious substantially solid piston of resilient material sealingly received within said body at its lower end beneath said injectable material and above said open bottom end, and a flexible reduced diameter extension integral with said piston, projecting downwardly from said piston but wholly within the body, for establishing a flexible connection to a syringe plunger in a zone between the piston and said open end of the body, whereby said vial may be converted into a syringe for ejection of the injectable material on movement of the piston towards the neck, by connection of said syringe plunger to said extension and connection of fluid conduit coupling means to said cylindrical cap, wherein the piston and its extension are formed of rubber of at least 50 durometer hardness, and the extension is formed with a central bore to increase its flexibility.

2. A vial according to claim 1, wherein the piston is formed with multiple axially spaced peripheral ribs in compressive engagement with an inside cylindrical wall of the vial body.

3. A syringe comprising a vial according to claim 1, an outer cap which is a push fit over the cap of the vial and incorporates a needle mounting adaptor concentric with said needle penetrable portion of the closure, and a tubular cylindrical syringe plunger for coupling to said flexible extension of the piston.

4. A syringe according to claim 3, further including an inwardly directed hollow needle received within the needle mounting adaptor, and a sleeve secured to an outer end of the needle projecting beyond the adaptor such that pressure on the sleeve when an injection needle is coupled to the adapter will force the hollow needle through the needle penetrable portion of the closure of a vial to which the outer cap is applied.

5. A vial formed of rigid transparent material and consisting of a cylindrical body, said body having an open bottom end having an external diameter at most only slightly greater than that of the remainder of the body, but sufficient relative to the height and center of gravity of the vial as a whole to support the latter in a stable manner when conveyed standing on its open end through vial filling and capping machinery, injectable material within the body, a comparatively wide neck at the top of the body through which said injectable material is filled into the body, an external peripheral flange surrounding the neck, an elastomeric closure applied to the neck, a cylindrical cap clamped onto the flange of the neck and having an annular inward extending flange at a top end overlaying the closure to secure the closure to the neck with the closure presenting a needle penetrable central portion, an impervious substantially solid piston or resilient material sealingly received within said body at its lower end beneath said injectable material and above said open bottom end, and a flexible reduced diameter extension integral with said piston, projecting downwardly from said piston but wholly within the body, for establishing a flexible connection to a syringe plunger in a zone between the piston and said open end of the body, whereby said vial may be converted into a syringe for ejection of the injectable material on movement of the piston towards the neck, by connection of said syringe plunger to said extension and connection of fluid conduit coupling means to said cylindrical cap; wherein the extension is formed with external screw threads for engagement with complementary threads on the plunger, and with abutment means to limit the distance through which the plunger can be screwed onto said threads, such as to prevent rigid abutment of the plunger against the piston and to enable the extension to form a flexible connection between the plunger and the piston.

6. A vial formed of rigid transparent material and consisting of a cylindrical body, said body having an open bottom end terminating in a peripheral bead having an external diameter at most only slightly greater than that of the remainder of the body, but sufficient relative to the height and center of gravity of the vial as a whole to support the latter in a stable manner when conveyed freestanding on said bead through vial filling and capping machinery, injectable material within the body, a comparatively wide neck at the top of the body through which said injectable material is filled into the body, an external peripheral flange surrounding the neck, an elastomeric closure applied to the neck, a cylindrical cap clamped onto the flange of the neck and having an annular inward extending flange at a top end overlaying the closure to secure the closure to the neck with the closure presenting a needle penetrable central portion, an impervious substantially solid piston of resilient material sealingly received within said body at its lower end beneath said injectable material and above said bead, and a flexible reduced diameter extension integral with said piston, projecting downwardly from said piston but wholly within the body, for establishing a flexible connection to a syringe plunger in a zone between the piston and said open end of the body, whereby said vial may be converted into a syringe for ejection of the injectable material on movement of the piston towards the neck, by connection of said syringe plunger to said extension and connection of fluid conduit coupling means to said cylindrical cap, wherein the weight of the piston and its extension is at least a major portion of that of the vial body, and the height of the vial body does not exceed about 2.5 times the external diameter of the bead.

7. A vial formed of rigid transparent material and consisting of a cylindrical body, said body having an open bottom end having an external diameter at most only slightly greater than that of the remainder of the body, but sufficient relative to the height and center of gravity of the vial as a whole to support the latter in a stable manner when conveyed standing on its open end through vial filling and capping machinery, injectable material within the body, a comparatively wide neck at the top of the body through which said injectable material is filled into the body, an external peripheral flange surrounding the neck, an elastomeric closure applied to the neck, a cylindrical cap clamped onto the flange of the neck and having an annular inward extending flange at a top end overlaying the closure to secure the closure to the neck with the closure presenting a needle penetrable central portion, an impervious substantially solid piston of resilient material sealingly received within said body at its lower end beneath said injectable material and above said open bottom end, and a flexible reduced diameter extension integral with said piston, projecting downwardly from said piston but wholly within the body, for establishing a flexible connection to a syringe plunger in a zone between the piston and said open end of the body, whereby said vial may be converted into a

syringe for ejection of the injectable material on movement of the piston towards the neck, by connection of said syringe plunger to said extension and connection of fluid conduit coupling means to said cylindrical cap,

wherein the closure substantially fills the neck of the body, and has a top flange overlying the neck and defines a central bore extending from the bottom of the closure to a point beneath said needle penetrable central portion, and wherein the closure further defines a cross bore extending from an outer wall of the closure beneath the flange to said central bore, whereby said cross bore and said central bore together constitute a vent from the interior of the vial when the closure is partially inserted in the neck of the vial body.

8. A syringe comprising:

A vial formed of rigid transparent material and consisting of a cylindrical body, said body having an open bottom end terminating in a peripheral bead having an external diameter at most only slightly greater than that of the remainder of the body, but sufficient relative to the height and center of gravity of the vial as a whole to support the latter in a stable manner when conveyed freestanding on said bead through vial filling and capping machinery, injectable material within the body, a comparatively wide neck at the top of the body through said injectable material is filled into the body, an external peripheral flange surrounding the neck, an elastomeric closure applied to the neck, a cylindrical cap clamped onto the flange of the neck and having an annular inward extending flange at a top end overlying the closure to secure the closure to the neck with the closure presenting a needle penetrable central portion, an impervious substantially solid piston of resilient material sealingly received within said body at its lower end beneath said injectable material and above said bead, and a flexible reduced diameter extension integral with said piston, projecting downwardly from said piston but wholly within the body, for establishing a flexible connection to a syringe plunger in a zone between the piston and said open end of the body, whereby said vial may be converted into a syringe for ejection of the injectable material on movement of the piston towards the neck, by connection of said syringe plunger to said extension and connection of fluid conduit coupling means to said cylindrical cap;

an outer cap which is a push fit over the cap of the vial and incorporates a needle mounting adaptor concentric with said needle penetrable portion of the closure; and

a syringe plunger for coupling to said flexible extension of the piston, wherein a tubular cylindrical front end of the syringe plunger is press fitted onto a front end of the outer cap to form a separately sterilized subassembly.

9. A syringe, comprising:

A vial formed of rigid transparent material and consisting of a cylindrical body, said body having an open bottom end terminating in a peripheral bead having an external diameter at most only slightly greater than that of the remainder of the body, but sufficient relative to the height and center of gravity of the vial as a whole to support the latter in a stable manner when conveyed freestanding on said bead through vial filling and capping machinery, injectable material within the body, a comparatively wide neck at the top of the body through which said injectable material is filled into the body, an external peripheral flange surrounding the neck, an elastomeric closure applied to the neck, a cylindrical cap clamped onto the flange of the neck and having an annular inward extending flange at a top end overlaying the closure to secure the closure to the neck with the closure presenting a needle penetrable central portion, an impervious substantially solid piston of resilient material sealingly received within said body at its lower end beneath said injectable material and above said bead, and a flexible reduced diameter extension integral with said piston, projecting downwardly from said piston but wholly within the body, for establishing a flexible connection to a syringe plunger in a zone between the piston and said open end of the body, whereby said vial may be converted into a syringe for ejection of the injectable material on movement of the piston towards the neck, by connection of said syringe plunger to said extension and connection of fluid conduit coupling means to said cylindrical cap;

an outer cap which is push fit over the cap of the vial and incorporates a needle mounting adaptor concentric with said needle penetrable portion of the closure; and

a syringe plunger having a tubular cylindrical end portion for coupling to said flexible extension of the piston;

wherein a piston stabilizer ring is a snap fit on the bead, the piston stabilizer ring having flanges extending into the vial body between the inner wall of the body and the plunger to limit tilting of the plunger and prevent withdrawal of the piston from the body.

10. A syringe comprising a vial formed of rigid transparent material and consisting of a cylindrical body, said body having an open bottom end having an external diameter at most only slightly greater than that of the remainder of the body, but sufficient relative to the height and center of gravity of the vial as a whole to support the latter in a stable manner when conveyed standing on its open end through vial filling and capping machinery, injectable material within the body, a comparatively wide neck at the top of the body through which said injectable material is filled into the body, an external peripheral flange surrounding the neck, an elastomeric closure applied to the neck, a cylindrical cap clamped onto the flange of the neck and having an annular inward extending flange at a top end overlaying the closure to secure the closure to the neck with the closure presenting a needle penetrable central portion, an impervious substantially solid piston of resilient material sealingly received within said body at its lower end beneath said injectable material and above said open bottom end, and an extension integral with said piston, projecting downwardly from said piston but wholly within the body, a needle mounting adaptor concentric with said needle penetrable portion of the closure, and an elongated syringe plunger for coupling to said flexible extension of the piston;

wherein the syringe plunger is moulded from synthetic plastic having hinge-forming capability, and has an outwardly extending flange at its rear end, a peripheral portion of this flange being separated form the remainder around about half of its circum-

ference, and the ends of the separated portion being connected to the remainder by integrally formed hinges to form a loop which can be pulled rearwardly of the flange.

11. A syringe plunger comprising an elongated stem defining a cylindrical recess at one end moulded from synthetic plastic material having hinge-forming capability, a cylindrical rubber piston of greater diameter than the plunger, an axial extension at one end of the piston entering within and releasably engaged with said cylindrical recess at one end of the plunger, and an outwardly extending flange at the other end of the plunger, a peripheral portion of this flange being separated from the remainder around about half of its circumference, and the ends of the separated portion being connected to the remainder by integral hinge-forming bridges to form a loop which can be pulled rearwardly of the flange.

* * * * *

EXHIBIT B

UNITED STATES INTERNATIONAL TRADE COMMISSION
WASHINGTON, D.C.

Before the Honorable Sidney Harris
Administrative Law Judge

In the Matter of	Investigation No. 337-TA-572
CERTAIN INSULIN DELIVERY DEVICES, INCLUDING CARTRIDGES HAVING ADAPTOR TOPS, AND COMPONENTS THEREOF	

RESPONDENTS' MOTION TO SANCTION COMPLAINANTS

Pursuant to Commission rule 210.4(d), 19 CFR § 210.4(d) and the inherent powers of the International Trade Commission ("ITC") to manage and administer the conduct of parties to ITC investigations and accepted principles of jurisprudence, Respondents Sanofi-Aventis Deutschland GmbH, Sanofi-Aventis, and Aventis Pharmaceuticals (collectively "Aventis" or "Respondents") respectfully move for an Order sanctioning Complainants Novo Nordisk A/S, Novo Nordisk Inc., and Novo Nordisk Pharmaceuticals Industries, Inc. (collectively "Novo" or "Complainants").

The bases for sanctioning Complainants are:

1. Complainants filed a Complaint lacking a good faith basis; and
2. When Respondents independently discovered Novo's prior art which invalidated the '027 patent in suit and requested a meet-and-confer on why Novo had not produced these prior art documents, instead of meeting and conferring Novo filed the motion to withdraw the Complaint.

Novo filed the Complaint in this investigation for the improper purposes of doing competitive harm to Aventis in the marketplace and of causing Aventis to expend money and other resources to defend, in violation of Commission Rule 210.4(c)(1). Novo caused the ITC to unknowingly serve improper purposes as Aventis had to spend money and other resources unnecessarily, and deal with the industry's fears that Aventis would be barred from importing and selling its OptiClik® system in the United States.

Novo did not produce its own prior art in response to Aventis' formal requests, and Aventis had to find those prior art references by an independent and costly investigation.

Wherefore, for the above reasons, as set forth in detail in the accompanying Response to Complainants' Motion to Withdraw and Memorandum in Support of Respondents' Motion for Sanctions, Aventis respectfully requests that an Order be entered that:

1. Novo pay Aventis for its costs of defending this investigation;
2. Novo be barred from asserting the '027 patent in a Complaint at the ITC;

3. Novo be barred from accusing Aventis' OptiClik® systems of infringement in a Complaint at the ITC; and

4. Novo be required to have any ITC Complaint it files in the next five (5) years be signed and certified by its Chief Executive Officer.

Date: Oct. 13, 2006

Respectfully submitted,

By: _____

Arthur Wineburg
Daniel E. Yonan
AKIN GUMP STRAUSS HAUER & FELD LLP
133 New Hampshire Ave. N.W.
Washington, D.C. 20036
Tel.: (202) 887-4000
Fax: (202) 887-4288

Paul H. Berghoff
David M. Frischkorn
Thomas E. Wettermann
MCDONNELL BOEHNEN HULBERT
& BERGHOFF LLP
300 South Wacker Drive
Chicago, Illinois 60606
Tel.: (312) 913-0001
Fax: (312) 913-0002

Attorneys for Respondents Sanofi-Aventis, Sanofi-Aventis Deutschland GmbH, and Aventis Pharmaceuticals Inc.

CERTIFICATE OF SERVICE

I HEREBY CERTIFY THAT ON OCTOBER 13, 2006, A COPY OF RESPONDENTS' MOTION TO SANCTION COMPLAINANTS

was served on the following as indicated:

Marilyn R. Abbott Secretary U.S. International Trade Commission 500 E Street, S.W., Room 112-F Washington, DC 20436	☒ Via Hand Delivery ☐ Via U. S. Mail ☐ Via Overnight Mail ☐ Via Electronic Mail ☐ Via Facsimile ☐ Via Electronic Docket Filing
The Honorable Sidney Harris U.S. International Trade Commission 500 E Street, S.W., Room 317 Washington, DC 20436	☒ Via Hand Delivery ☐ Via U. S. Mail ☐ Via Overnight Mail ☐ Via Electronic Mail ☐ Via Facsimile ☐ Via Electronic Docket Filing
Juan Cockburn, Esq. Office of Unfair Import Investigations U.S. International Trade Commission 500 E Street, S.W., Room 401 Washington, DC 20436	☒ Via Hand Delivery ☐ Via U. S. Mail ☐ Via Overnight Mail ☒ Via Electronic Mail ☐ Via Facsimile
Delbert R. Terrill, Jr., Esq. Joanna M. Ritcey-Donohue, Esq. Todd P. Taylor, Esq. White & Case LLP 701 Thirteen Street, NW Washington, DC 20006	☒ Via Hand Delivery ☐ Via U. S. Mail ☐ Via Overnight Mail ☒ Via Electronic Mail ☐ Via Facsimile
Jeffrey J. Oelke, Esq. Scott T. Weingaertner, Esq. White & Case LLP 1155 Avenue of the Americas New York, NY 10036	☐ Via Hand Delivery ☒ Via U. S. Mail ☐ Via Overnight Mail ☒ Via Electronic Mail ☐ Via Facsimile

Melanie Hayes
Paralegal